RESERVE

VOL. CLIV, No. 1 JULY, 1917 No. 544

ESTABLISHED 1820

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

THE LIBRARY OF THE UNIVERSITY OF PENNSYLVANIA MEDICAL DEPARTMENT JUN 3 1944

GEORGE MORRIS PIERSOL, M.D., EDITOR

JOHN H. MUSSER, JR., M.D., ASSISTANT EDITOR

RESULTS OF DEEP ROENTGEN-RAY TREATMENT IN 258 CASES OF MALIGNANT TUMORS. By ARTHUR FENWICK HOLDING, M.D. 1

SYPHILITIC AORTITIS. By ARTHUR R. ELLIOTT, M.D. 14

CONGENITAL ABSENCE OF LUNG. By A. G. ELLIS, M.D. 33

THE USE OF IMMUNE SERUM IN THE TREATMENT OF WHOOPING COUGH. By ADRIEN BLEYER, M.D. 39

AURICULAR FIBRILLATION: SOME CLINICAL CONSIDERATIONS. By SAMUEL A. LEVINE, M.D. 43

TYPHOID MENINGITIS: WITH REPORT OF A CASE. By STANHOPE BAYNE-JONES, M.D. 55

VISCERAL FINDINGS IN ONE HUNDRED SYPHILITICS. By TASKER HOWARD . . 64

PULSATING SPLEEN IN MITRAL AND TRICUSPID DISEASES. By MORRIS MANGES, M.D. 72

THE RATE OF EXCRETION OF THE THREE NITROGENOUS WASTE PRODUCTS, URIC ACID, UREA AND CREATININ IN NEPHRITIS, AS SHOWN BY COMPARATIVE STUDIES OF THE BLOOD AND URINE. By C. K. WATANABE, M.D. 76

A CLINICAL STUDY OF CHLORIDE EXCRETORY FUNCTION. By C. C. WOLFERTH, M.D. 84

FAMILIAL EPISTAXIS: A CASE REPORT. By HENRY B. RICHARDSON, M.D. 95

DIAGNOSIS OF EARLY PULMONARY TUBERCULOSIS. By JAMES I. JOHNSTON, M.D. . 100

THE INFLUENCE OF RENAL FUNCTION OF HYPERGLYCEMIA AND GLYCOSURIA IN DIABETES MELLITUS. By ALBERT A. EPSTEIN, M.D. 103

SURGEON GENERAL'S OFFICE BULLETIN . . . . ADVERTISEMENT PAGE 15

(Contents continued on page iv)

OWNERS AND PUBLISHERS

Philadelphia LEA & FEBIGER New York

COPYRIGHT, 1917, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, FIVE DOLLARS A YEAR, POSTPAID

KAYESS PRODUCTS

It is hard to tell which feature of the Silent "KAYESS" X-Ray Transformer will appeal to you most.

Perhaps you will consider the absence of moving parts its principal feature. There is nothing to wear out on the Silent "KAYESS."

Or, you may be more deeply impressed by the fact that accessory devices are not required. There is nothing to become deranged.

Or, you can consider it an ideal investment because it involves no maintenance cost. No further expenditure is necessary.

And we can assure you in advance that actual experiment with the machine will prove a revelation. Its splendid Radiographic results in bone details and soft-tissue work show a larger percentage of finer details than any known apparatus.

But there is just the possibility that you will select it because of its flexibility and power. It can be instantly controlled, you know, from the smallest milliampèrage to a heavy discharge for instantaneous radiography with any amount of intermediate steps.

In any event you will be choosing the most efficient piece of X-ray mechanism now available—

As the Silent "KAYESS" Booklet Proves
a copy of which is yours for the asking

MANUFACTURED BY

THE KNY-SCHEERER CORPORATION

X-Ray and Electro-Medical Department

404-410 WEST 27TH STREET, NEW YORK

W
fo

Li

ntage

of its
n the
raphy

X-ray

Which Mineral Oil is Best for Medical and Surgical Use

?

1. That oil which is free from paraffin and all toxic, irritating or otherwise undesirable elements, such as anthracene, phenanthrene, chrysene, phenols, oxidized acid and basic bodies, organic sulphur compounds and foreign inorganic matter; because an oil of such purity will pass through the gastro-intestinal tract without causing irritation or other untoward effects.

2. That oil which possesses the highest natural viscosity, with the highest specific gravity, because such an oil will pass through the intestine more slowly than a lighter and thinner oil and lubricate the walls of the gut more completely, and soften fæces more effectually, and is not likely to produce dribbling.

3. That oil which is really colorless, odorless and tasteless, because palatability favors persistence in treatment.

The oil which meets all these requirements is

Liquid Petrolatum, Squibb

Heavy (Californian)

It is a pure, colorless, odorless and tasteless MINERAL OIL, specially refined under our control only by the *Standard Oil Company* of *California* which has no connection with any other Standard Oil Company. This oil has the very high specific gravity of 0.886 to 0.892 at 15°C. (or 0.881 to 0.887 at 25°C.) and has also an exceptionally high natural viscosity. It is sold solely under the Squibb label and guaranty and may be had at all leading drug stores.

E. R. SQUIBB & SONS, NEW YORK

KALMERID—An improved catgut superseding iodized sutures
DAVIS & GECK, INC., Brooklyn, NY, U.S.A.

THE GRADUATE SCHOOL OF THE UNIVERSITY OF MINNESOTA

offers

Graduate Instruction in Medicine on a University Basis

in The Medical School of the University
and in The Mayo Foundation for Medical Education and Research

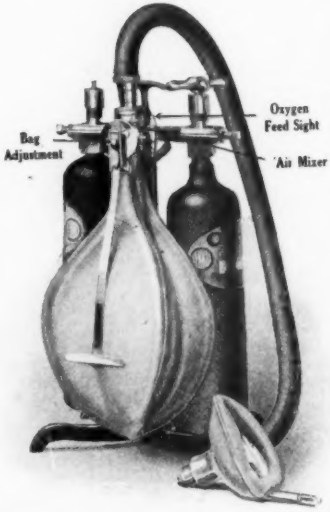
For details as to requirements for admission, residence, tuition and paid Fellowships, address

THE DEAN OF THE GRADUATE SCHOOL
UNIVERSITY OF MINNESOTA
MINNEAPOLIS, MINN.

or

THE MAYO FOUNDATION FOR
MEDICAL EDUCATION AND RESEARCH
ROCHESTER, MINN.

The McKesson Apparatus



The McKesson Apparatus is manufactured in several types for various purposes.

The cut illustrates our obstetrical machine—THE JUNIOR.

We also make the Model F Automatic Apparatus for major surgery, obstetrics and dentistry. It is constructed to meet every requirement of the anesthetist and to produce those ideal gas-oxygen results in the simplest, surest and easiest possible manner.

Write for full description, prices, etc.

TOLEDO TECHNICAL APPLIANCE COMPANY

TOLEDO, OHIO

BACK COPIES American Journal of Medical Sciences and other Medical Periodicals, Domestic and Foreign, as well as complete sets.

Books on History of Medicine and Books of the older Medical Authors.

For Sale by B. LOGIN & SON, 152 East 23d St., New York City

No Connection with any other firm of same name.

"Sutures fit for Surgery"
DAVIS & GECK, INC. Brooklyn, NY, U.S.A. KALMERID

Stanolind

Trade Mark Reg. U. S. Pat. Off.

Liquid Paraffin

(Medium Heavy)

Tasteless — Odorless — Colorless

In Treating Hemorrhoids

STANOLIND Liquid Paraffin, used regularly, very generally relieves hemorrhoids and fissure, even when of some years' standing.

Since these morbid conditions are usually the result of constipation, and are aggravated by straining, Stanolind Liquid Paraffin aids by rendering the intestinal contents less adhesive, by allaying irritation and thus by permitting the diseased tissues to become healed.

Where a contraindication for operative treatment exists, the use of Stanolind Liquid Paraffin in these conditions will frequently give relief from distressing symptoms and may even permit the parts to be restored to a condition where operative procedure may be postponed.

The ***special advantage*** of Stanolind Liquid Paraffin lies in the fact that its beneficial effects are not diminished by continual use, as is the case with almost any other laxative.

Stanolind Liquid Paraffin acts by lubrication and by adding bulk to the indigestible intestinal residue.

A trial quantity with informative booklet will be sent on request.

Standard Oil Company

72 West Adams Street (*Indiana*) Chicago, U. S. A.

75a

CONTENTS

ORIGINAL ARTICLES

Results of Deep Roentgen-ray Treatment in 258 Cases of Malignant Tumors 1

By Arthur Fenwick Holding, M.D., New York.

Syphilitic Aortitis 14

By Arthur R. Elliott, M.D., Chicago.

Congenital Absence of Lung 33

By A. G. Ellis, M.D., Philadelphia.

The Use of Immune Serum in the Treatment of Whooping Cough . . 39

By Adrien Bleyer, M.D., St. Louis.

Auricular Fibrillation: Some Clinical Considerations 43

By Samuel A. Levine, M.D., Boston.

Typhoid Meningitis: With Report of a Case 55

By Stanhope Bayne-Jones, M.D., Baltimore, Maryland.

Visceral Findings in One Hundred Syphilitics 64

By Tasker Howard, Brooklyn, N. Y.

Pulsating Spleen in Mitral and Tricuspid Diseases 72

By Morris Manges, M.D., Professor of Clinical Medicine, University and Bellevue Hospital Medical College; Visiting Physician, Mount Sinai Hospital, New York.

The Rate of Excretion of the Three Nitrogenous Waste Products, Uric Acid, Urea and Creatinin in Nephritis, as Shown by Comparative Studies of the Blood and Urine 76

By C. K. Watanabe, M.D., New York.

A Clinical Study of Chloride Excretory Function 84

By C. C. Wolferth, M.D., Philadelphia.

Familial Epistaxis; a Case Report 95

By Henry B. Richardson, M.D., Boston.

(*Continued on page 6*)

WAPPLER

HIGH FREQUENCY MACHINES

have been recommended as the Standard by the American Electro-Therapeutic Association.

Made in Seven Models, $75 up

Use our "DIATHERMIC" Machine for Heating the Blood Stream

Any Electro-Medical Apparatus from a Roentgen-Ray Plant to a Diagnostic Light Controller is reliable if it bears the name of

WAPPLER

"EXCELL"
HIGH FREQUENCY MACHINE

Correspondence relative to these machines and other Electro-Medical apparatus is invited.

PLEASE ADDRESS H. F. DEPARTMENT

WAPPLER ELECTRIC CO., Inc.

173-175 East Eighty-seventh Street ∴ NEW YORK

CONTENTS—(*Continued*)

Diagnosis of Early Pulmonary Tuberculosis 100

By JAMES I. JOHNSTON, M.D., Physician to the Mercy Hospital, Pittsburgh, and Assistant Professor of Medicine in the University of Pittsburgh Medical School.

The Influence of Renal Function on Hyperglycemia and Glycosuria in Diabetes Mellitus 103

By ALBERT A. EPSTEIN, M.D., Adjunct Attending Physician and Assistant Physiological Chemist, Mount Sinai Hospital, New York.

REVIEWS

Fractures and Dislocations. By L. A. Stimson, B.A., M.D., LL.D. . . 122
Surgical Operations. By Krause, Heyman and Ehrenfried 123
A Text-book of Histology. By Frederick R. Bailey, A.M., M.D. . . 123
The Pathology of Nephritis. By William Ophüls 124
Bone and Joint Studies. By Leonard W. Ely and John Francis Cowan . 124
Principles of Treatment of Broken Limbs. By William F. Fluhrer . . 124
A Practical Medical Dictionary. By Thomas Lathrop Stedman, A.M., M.D. 125
A Text-book of Pathology. By Alfred Stengel, M.D., Sc.D., and Herbert Fox, M.D. 125
Diseases of the Stomach, Intestines and Pancreas. By Robert Coleman Kemp, M.D. 126
Diagnosis and Treatment of Abnormalities of Myocardial Function. By T. Stuart Hart, A.M., M.D. 126
A Treatise on Diseases of the Skin. By Henry W. Stelwagon, M.D., Ph.D. 127
Fats and Fatty Degeneration. By Martin H. Fischer, M.D., and Martin O. Hooker, M.D. 127
The Physiology of the Amino-acids. By Frank P. Underhill, Ph.D. . . . 128

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D., AND ROGER S. MORRIS, M.D.

d-Glucose Tolerance in Health and Disease 129
Septicemia due to Micrococcus Tetragenus 130
Results of Treatment of Hodgkin's Disease 131

(*Continued on page 8*)

DIAGNOSTIC INSTRUMENTS

Electrically lighted surgical instruments bearing the stamp E. S. I. Co. are designed by eminent physicians and are warranted mechanically and electrically perfect:

Holmes Naso-Pharynogscope
Jackson Bronchoscopes and Laryngeal Specula
Tuttle and Lynch Procto-Sigmoidoscopes
Braasch Cystoscopes
Koch, Swineburne and Young Urethroscopes

Accurate Diagnosis is Assured

Origination Begets Imitation
For your protection be sure every instrument is marked "E. S. I. Co."

A Modern Diagnostic Outfit

This outfit will be found both compact and convenient. It weighs but 4½ pounds and measures 3½ x 7 x 15 inches and is easily carried. It consists of

1 Auriscope and Nasoscope combined
1 Tongue Depressor
2 Koch Urethroscopes (any sizes)
1 Light Carrier for Urethroscopes (interchangeable)
1 E. S. I. Co. Socket Controller instead of Battery, if desired
1 Tungsten Battery with Conducting Cord
1 Laryngoscope
1 General Diagnostic Illuminator
1 E. S. I. Co. Proctoscope
1 Light Carrier for Proctoscope

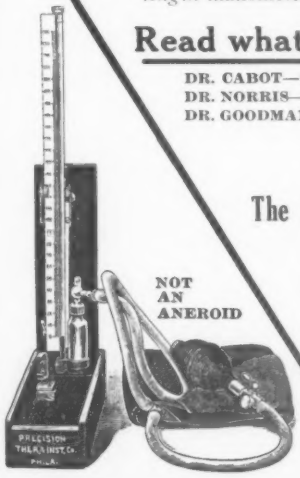
A copy of illustrated and descriptive **Catalogue** *will be sent upon request*

Electro Surgical Instrument Company
Rochester, N. Y.

THOUGHTFUL PHYSICIANS are using the

Nicholson Princo Sphygmomanometer

The *folding pocket mercurial* instrument with the *full length* manometer tube and scale graduated in single mm.



NOT AN ANEROID

Read what they say:

DR. CABOT—"Physical Diagnosis." Pages 107-110
DR. NORRIS—"Blood-Pressure, its Clinical Application." Page 132
DR. GOODMAN—"Blood-Pressure in Medicine and Surgery." Page 56

PRICE $18.00

The Instrument with the *Steel* Reservoir

Our little booklet "Blood-Pressure" contains a complete description of this instrument. We'll be glad to send you a copy along with a pamphlet on the Clinical Significance of Diastolic and Pulse Pressure. Free for the asking.

Precision Thermometer & Instrument Co.
1434 Brandywine Street
PHILADELPHIA, PA.

CONTENTS—(*Continued*)

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.

Principles of the Transfusion of Blood 133
Surgery of Amputation Stumps, Based on the Experience of 2000 Consecutive Cases 133
Results of Local Anesthesia in Prostatectomy 134
Scoliosis (Treatment) 134
Pernicious Anemia, with Special Reference to its Surgical Management . 135

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Study of Ethylhydrocuprein (Optochin) in the Treatment of Acute Lobar Pneumonia 136
Effects of Salicylates on Experimental Arthritis in Rabbits 136
Treatment of Tuberculosis with Cyanocuprol 137
Nutritional Value of the Banana 137
Salvarsan and Neosalvarsan in Syphilis 138
Transfusion of Blood 139
Passage of Neutralizing Substances from the Blood into the Cerebrospinal Fluid in Poliomyelitis 140
Lumbar Puncture for the Relief of Delirium in Lobar Pneumonia . . 140

OBSTETRICS

UNDER THE CHARGE OF

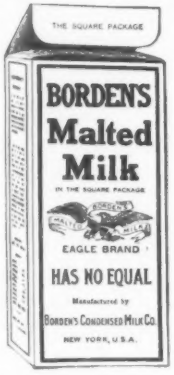
EDWARD P. DAVIS, A.M., M.D.

Morphin-scopolamin during Labor 141
Pyelitis in Pregnancy and Parturient Women 141
Cases of Apparent Appendicitis Complicating Pregnancy 142
Morphin-hyoscin Method of Painless Childbirth 143
Joined Twins 144
Combination of Morphin and Pituitrin in Labor 145

(*Continued on page 10*)

The History of Malting Milk

BARON VON LIEBIG originated the process for malting milk in Germany over 50 years ago. Countess von Ebersburg obtained an English patent in 1867 covering von Liebig's process for a preparation in either liquid form for immediate use or a dried state for future use. This patent called for skimmed milk and the product was not as perfect as that manufactured and sold to-day under the name of



BORDEN'S
Malted Milk
IN THE SQUARE PACKAGE

This product, while containing all the good features of the von Liebig process and the von Ebersburg patent, uses the best full-cream cows' milk in its manufacture. The improved vacuum process of condensing (without impairment of food value) originated by GAIL BORDEN, the founder of this company, is also used in the manufacture of this Malted Milk which won the

Grand Prize Highest Award Panama Expositions

ANOTHER PROOF OF QUALITY

NEW (8th) EDITION **JUST READY** **THOROUGHLY REVISED**

A PRACTICAL TREATISE ON

FRACTURES and DISLOCATIONS

By LEWIS A. STIMSON, B.A., M.D., LL.D.

Professor of Surgery in Cornell University Medical College, New York; Consulting Surgeon to New York and Bellevue Hospitals; Corresponding Member of the Société de Chirurgie of Paris.

Octavo, 946 pages, with 475 illustrations and 39 plates. Cloth, $6.00, net.

The splendid record achieved by this work is evidenced in the appearance of its eighth edition. The author, who is the greatest living authority on fractures and dislocations, has again performed the work of revision with extreme thoroughness, incorporating in the text the accumulated experience and the new methods which have been perfected in recent years in the treatment of fractures.

The war in Europe has brought to the hospitals an enormous number of fractures and fixed upon them the attention of surgeons to an unprecedented extent. In the course of two visits to France Dr. Stimson saw much of this work and noted the various methods. Many interesting details have been set forth in this new edition. In the formulation of principles and indication of choice of methods it should be a safe guide for the practitioner and student.

706-8-10 Sansom St. PHILADELPHIA **LEA & FEBIGER** PUBLISHERS 2 W. 45th Street NEW YORK

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

Surgical Traumatism as a Cause of Recurrence in Uterine Carcinoma . 145
Operation for Uterine Prolapse 146
Hernia of the Bladder 146

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P., AND OSKAR KLOTZ, M.D., C.M.

Concerning Renal Sclerosis 147
Diminution of the Number of Islands of Langerhans in Diabetes . . . 147
Studies of the Betahemolytic Streptococci 148
Observations on the Mode of Origin of the Fibro-adenoma of the Mammary Gland in the Rat and on the Delayed Retrogression of the Mammary Gland after the Period of Lactation 149
Study of Experimental Non-hemolytic Streptococcus Lesions in Vitally Stained Rabbits 150
Contribution to the Epidemiology of Lobar Pneumonia 151

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D., AND JOHN F. ANDERSON, M.D.

Studies of the β-hemolytic Streptococcus 152
Influence of Milk and Carbohydrate Feeding on the Character of the Intestinal Flora. Diet versus Bacterial Implantation 153
Clarification of Milk 154
Is Mosquito or Man the Winter Carrier of Malaria Organisms? . . . 154
Laundries and the Public Health 155

LEDERLE'S POLLEN VACCINE

In the Prophylaxis and Treatment of

HAY-FEVER

In 1915, **Lederle's Pollen Vaccine** was used by over 600 physicians for the prophylaxis and treatment of hay-fever. A clinical history blank was submitted to each physician and the results of the collected data are as follows:

1. Favorable results followed as a **prophylactic** against hay-fever in **83 per cent.** of the cases.
2. In the **treatment** of hay-fever favorable results followed in **89 per cent.** of the cases.
3. Marked asthmatic symptoms were associated with 55 per cent. of the cases. The symptoms were relieved in 84.2 per cent. of the cases.

During 1916, **Lederle's Pollen Vaccine** was employed by over 1500 physicians with the following results:

1. Favorable results followed as a **prophylactic** in **80 per cent.** of the cases.
2. In the **treatment** of hay-fever favorable results were obtained in **91.7 per cent.** of the cases.
3. Marked asthmatic symptoms were associated with 53 per cent. of the cases. These symptoms were successfully relieved in 78.5 per cent. of the cases.

Lederle's Pollen Vaccine was used with favorable results in 40 states of the Union; from Maine to California; and as far away as Porto Rico.

The above results in the prophylaxis of hay-fever are based on the use of **Lederle's Pollen Vaccine** according to our original recommendation of 15 doses for the complete treatment.

Literature will be sent to any physician upon request

LEDERLE ANTITOXIN LABORATORIES

SCHIEFFELIN & CO., Distributors

NEW YORK

MULFORD
FOR THE CONSERVATION OF LIFE
LABORATORIES

Fall Hay Fever

Hay Fever Pollenin Fall Mulford

(Formerly Hay Fever Vaccine Mulford)

is indicated in the prevention and treatment of Fall Hay Fever. **Hay Fever Pollenin Fall Mulford** contains the protein extracts obtained from the pollens of ragweed, golden-rod and corn, and is indicated in hay fever occurring in persons susceptible to the several pollens.

Hay Fever Pollenin Ragweed Mulford

(Formerly Hay Fever Vaccine Ragweed Mulford)

consists of the protein extract obtained from the pollen of ragweed—the cause in a majority of cases of hay fever occurring in the Fall—dissolved in physiological saline solution and accurately standardized.

Hay Fever Pollenin Fall Mulford and **Hay Fever Pollenin Ragweed Mulford** are furnished in:

Packages containing 4 sterile glass syringes of graduated strengths, $5.00
In single syringes "D" strength, $1.50

Syringe A contains 0.0025 mg. extract of the pollen proteins
" B " 0.005 " " " " " "
" C " 0.01 " " " " " "
" D " 0.02 " " " " " "

In ordering specify "Hay Fever Pollenin Fall" or "Hay Fever Pollenin Ragweed" as may be desired, otherwise the Hay Fever Fall Pollenin will be supplied.

For Immunization and Treatment of Hay Fever, first dose (Syringe A) should be given at least 30 days before expected attack, followed by syringes B, C and D at five-day intervals; during the entire period of accustomed attack or until immunity is established treatment should be continued, using Syringe D.

There are no contraindications to the therapeutic or prophylactic use of Hay Fever Pollenin Mulford as far as known. Should a clinical reaction occur, characterized by rise in temperature and aggravation of symptoms, the next dose should be decreased.

Full literature mailed upon request.

H. K. MULFORD CO., Philadelphia, U. S. A.

27182 **Manufacturing and Biological Chemists**

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JULY, 1917

ORIGINAL ARTICLES

RESULTS OF DEEP ROENTGEN-RAY TREATMENT IN 258 CASES OF MALIGNANT TUMORS.

By Arthur Fenwick Holding, M.D.,

NEW YORK.

(From the Memorial Hospital, New York City.)

During the past four years we have had the opportunity of studying the action of roentgen rays with and without other adjuvant methods in a series of 658 cases of malignant tumors and allied conditions referred to the roentgen department of the Memorial Hospital. In summarizing these results, and as a basis for this paper, we have selected 258 cases in all of which the microscopic diagnosis and clinical data were established beyond question. Outside of the cases of Hodgkin's disease it will be seen that the cases treated represent what is commonly recognized as true cancer, and therefore the study of these cases will serve to indicate what results we can logically expect to attain in treating this class of cases with the roentgen rays at the present time. *No endeavor has been made to feature the few cases that responded unusually well to treatment,* and we have eliminated from our lists all cases in which the diagnosis was not verified by competent microscopic examination, all cases in which the clinical data and subsequent histories were incomplete, and cases that discontinued treatment, etc.; also all cases of uterine carcinoma as they will be reported by the gynecological department. The cases were classified as follows:

	Total.	Improved.	Unimproved.	P. I.—8. D.	Improved; still under treatment.	Dead.
EPITHELIAL TISSUE.						
1. Basal-cell epithelioma	16	16	0	0	16	0
2. Squamous-cell epithelioma	38	5	33	4	1	37
3. Alveolar and scirrhus carcinoma of breast	59	32	27	18	14	45
4. Carcinoma of testis (teratoid)	5	5	..	3	..	5
5. " of neck (branchial clefts)	7	..	7	..	..	7
6. " of esophagus	1	..	1	..	..	1
7. " of stomach	2	..	2	..	..	2
8. " of intestines (carcinosis)	4	..	4	..	..	4
9. " of colon	4	1	3	1	..	4
10. " of rectum	7	..	7	..	..	7
11. " of thyroid	5	4	2	3	1	5
12. " of lung	3	1	2	1	..	3
13. " of tonsil	1	..	1	..	..	1
14. " of ovary	2	1	1	..	1	1
15. " of larynx	6	..	6	..	..	6
16. " of gall-bladder	1	1	..	1	..	1
17. Melanoma	4	1	3	1	..	4
CONNECTIVE TISSUE.						
18. Sarcoma, mixed, myeloid, spindle, etc.	38	6	32	4	2	36
19. Sarcoma, melano	4	1	3	1	..	4
LYMPHATIC TISSUE.						
20. Sarcoma, lympho	21	15	6	8	7	14
21. Pseudo leukemia	12	10	2	3	7	5
22. Lymphatic leukemia, chronic	4	3	1	2	1	2
23. Splenomyelogenous leukemia	2	2	..	2	..	2
24. Lymphoma	1	1	..	1		
25. Thymoma	1	1	..	..	1	
OTHER TISSUES.						
26. Mixed tumors (parotid)	1	..	1	..	..	1
27. Endothelioma	1	..	1	..	..	1
28. Glioma retina	1	..	1			
29. Lipoma recurrent	1	1				
30. Rhabdomyo sarcoma	1	..	1	..	..	1
31. Hypernephroma	1	..	1	..	..	1
32. Adamantenoma	1	..	1			
33. Embryonal carcinoma	2	1	..	1	1	1
	258	108	150	54	54	203

EXPLANATION OF CLASSIFICATION. In most of our cases "improved" means a diminution in the size of the lesions, with a diminution of the symptoms. If the lesions were ulcerative in character there were evidences of healing best shown in early cases of basal-cell epithelioma, in which the healing was uniformly prompt, progressive, and complete, except in late and very extensive lesions. If the lesions were subcutaneous or metastatic, "improved" means that they diminish in size.

2536 C 1

29 My 44

Pain was very strikingly relieved in many of the cases; discharge diminished in quantity and odor. If the patient's symptoms improved, but the lesions did not show improvement, the case was not considered improved.

"Unimproved" means that the patient's lesions or symptoms or both were not improved and that the lesions steadily progressed despite treatment.

Some of the cases showed such marked improvement under treatment at first that although they subsequently died it was deemed important to call attention to this class of cases by tabulating them under the heading of "primarily improved, subsequently died." Our experience has led us to expect certain cases to do very well under treatment at first and raise great hopes of recovery in the patient and the therapeutist. Such cases have frequently been reported in the literature during this stage of improvement, and not uncommonly the patients have relapsed and died by the time the reports have been published. Some cases are improved but still under treatment, so that their ultimate results are not known. These are classified in the column "improved, still under treatment."

Apparatus and Technic. The apparatus and technic used in administrating the roentgen-ray dosage consists of a high-tension transformer capable of giving sparks 10 inches long between the poles of the spark gap, while the Coolidge tube is in operation (this high-tension transformer is run by the 220 volt alternating current) broad focussed Coolidge tubes regulated so as to back up a 10-inch parallel spark gap while in operation and passing 7 milliampères of current through the tube. The focus skin distance was 6 to 8 inches, the rays were filtered through 3 mm. of aluminum in the early treatments and through 4 mm. of aluminum later in the series. The dosage was measured on the skin by means of Corbett's modification of the Lovibund tintometer. Our average skin dose is 3 B Saboreaud, equivalent to 15 Holtzknecht or 30 Kienbock units to each area treated. The average time required to obtain this dose was 3 to 4 minutes.

The roentgen rays were applied through portals varying from 3 to 5 cm. square, using the cross-fire method of traversing the diseased tissues at many angles. The maximum dose for skin toleration was administered as shown by the tintometer readings and verified by the erythemas produced. The dosage was never repeated over a given area at intervals of less than two weeks. We found that we could treat 2 to 3 portals at a sitting without causing nausea in our patients, but treating a greater number of portals always caused depression and nausea even when the patients were under alkaline treatment to overcome acidosis. When treating directly over the stomach the patients were prone to become extremely nauseated. To illustrate the number of portals used, let us take for example a

case of carcinoma of the breast, in which we would select the following portals:

Anterior chest, 2 to 4 portals.
Posterior chest, 2 to 4 portals.
Axilla and axillary line, 1 to 2 portals.
Supraclavicular fossa and neck, 1 to 2 portals.
Total, 6 to 12 portals over each side of the thorax.

In selected cases both mammary regions were treated through these multiple portals. Attempts were made to increase the skin dosage tolerance by various methods of dehematizing the skin

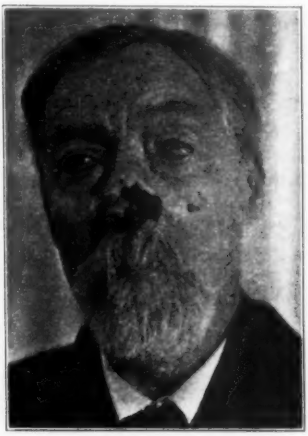


FIG. 1.—Before treatment.

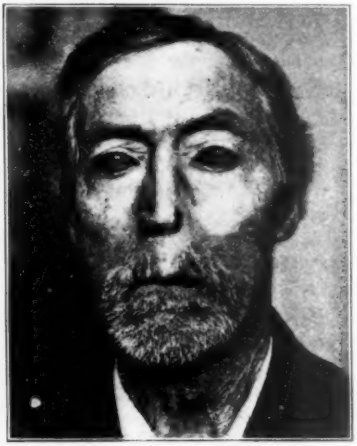


FIG. 2.—After treatment.

FIGS. 1 and 2.—Microscopic diagnosis: basal epithelioma. Duration, fourteen years. Previous treatments: local applications of ointments, pastes, caustics, curettement, high-frequency current, etc. Occupation: farmer. Preëpithelial keratoses are scattered over face, neck, and hands. Two treatments improved the patient so much that he discontinued treatments for seven months, believing himself well. On his return it required seven more treatments over the nose to control the condition and eight treatments to clear the face, neck, and hands of the keratoses.

through pressure, ice-bags, and adrenalin injections, but without sufficient success to make us feel warranted in continuing them. Attempts were also made to increase the number of secondary rays generated in the tumors by injecting suspensions of heavy metals and also by producing hyperemia within the tumors. These attempts were not attended with any noteworthy success. The application of heat by diathermy in conjunction with the roentgen rays was tried, and it appears to be a synergist to the roentgen-ray treatment in superficial cases and in those cases in which the heat acted practically as a removal by cautery. When sloughing obtained, however, in these cases the wounds were sluggish in healing.

INTERPRETATION OF THE THERAPEUTIC RESULTS. *Basal-cell Epithelioma.* Except in old advanced cases the results in this type of lesion are uniformly good, all 16 cases responding promptly, the lesions healing in from three to twelve weeks, and with one exception have remained well to date. With proper microscopic diagnosis other more painful methods are unnecessary.

Squamous-cell Epithelioma. The bad results in this class of cases are in marked contrast to the good results obtained in basal-cell epithelioma. The one improved case shown in the table of cases was treated with the roentgen rays combined with diathermic coagulation. He was symptomatically well for six months and then showed signs of local recurrence. He was again treated with massive doses of roentgen rays locally and roentgen rays cross-fired through the cervical lymph nodes. The condition seems to be under control at the present time, but the prognosis is dubious. This is a good illustration of the course of squamous epithelioma under treatment.

Carcinoma of the Breast. A majority of these cases show a primary improvement evidenced by diminution in the size of the tumors, both primary and metastatic, with frequent disappearance of the latter. Diminution in pain, discharge and fetor are also notable. Metastases are always more amenable to roentgen therapy than primary growths, and the earlier they are treated after their appearance the more evident this becomes. Efficient treatment of early metastases may cause a complete clinical disappearance of cancer tissue. In cases in which the therapeutic effect of the ray has not entirely succeeded, careful search will usually reveal small groups of viable cells, accounting thereby for such local recurrences as do occur. Besides the primary lethal effect of the ray on the malignant cells we have to do in all probability with a second and very important factor in determining the success or failure of our method of treatment. That is the degree in which the stroma has gone in supplying the necessary circulation for the cells of the growth, for where these cells have time to be provided with abundant stroma, containing a rich blood supply, it seems more difficult to eradicate the cancer cells entirely. It is for this reason, we believe, that metastases are more influenced than primary growths and why early metastases can be obliterated entirely. We believe that the greatest emphasis should be laid on the value of the preoperative and postoperative raying in all cases, in which surgical removal is contemplated, because the surgeon can never feel assured that he has not left behind isolated cells. And if these cells are to be attacked successfully, the time to do it is, we believe, when they are not connected organically with the circulation of the host.

Lymphosarcoma. This class of cases gives us our most brilliant primary results. In many cases the tumors melt away and there is a notable restoration of health and sense of well-being. Unfortu-

nately in our experience they all relapse and the process proceeds despite all treatment.

Lymphoid Group. In pseudoleukemia, chronic lymphatic leukemia, splenomyelogenous leukemia, lymphoma we see the same result as in lymphosarcoma; primary improvement with disappearance of the tumors is the rule. Ultimately these cases relapse and die. In thymoma, however, we have had good results which have lasted to date. What the ultimate result will be we cannot at present state, but in this one group we are optimistic.

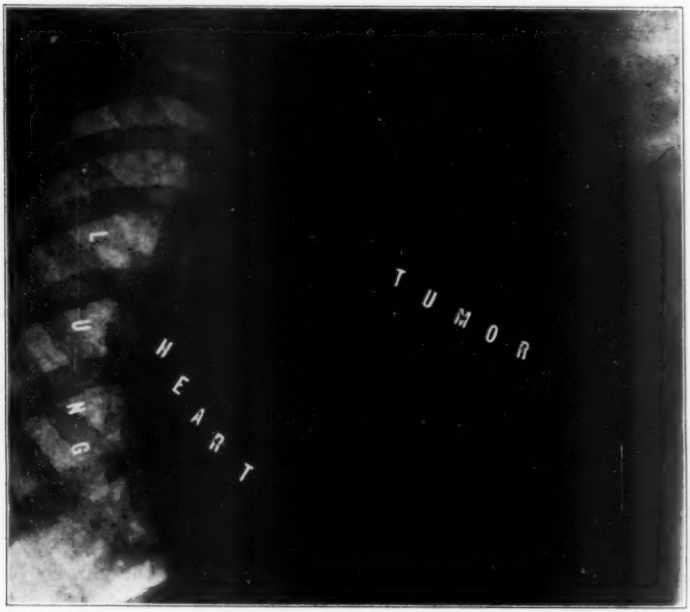


FIG. 3.—Embryonal carcinoma of the left lung before treatment, January 12, 1915.

Carcinoma of the Viscera. All failed to show noteworthy improvement except carcinoma of the thyroid and adenocarcinoma of the ovary. One case of large inoperable adenocarcinoma of the ovary involving the omentum and viscera was given three times our maximum dose of roentgen rays through an open wound and in the abdomen. All evidences of the tumor disappeared subsequent to this for a period of nine months. The patient then returned to the hospital in a feeble condition with evidence of widespread pelvic adhesions. She was given as much roentgen-ray treatment as her feeble condition warranted. She finally died in a very much emaciated condition and with symptoms of obstruction of the bowels. At autopsy there were no evidence of any carcinoma in the pelvis

whatever; all had disappeared and been replaced by connective tissue. There were extensive metastases in the liver and spleen.

Embryonal Carcinoma. In our series we had 2 cases of embryonal carcinoma. They showed very marked initial improvement. One relapsed despite all treatment; the other is still in the initial improvement stage.

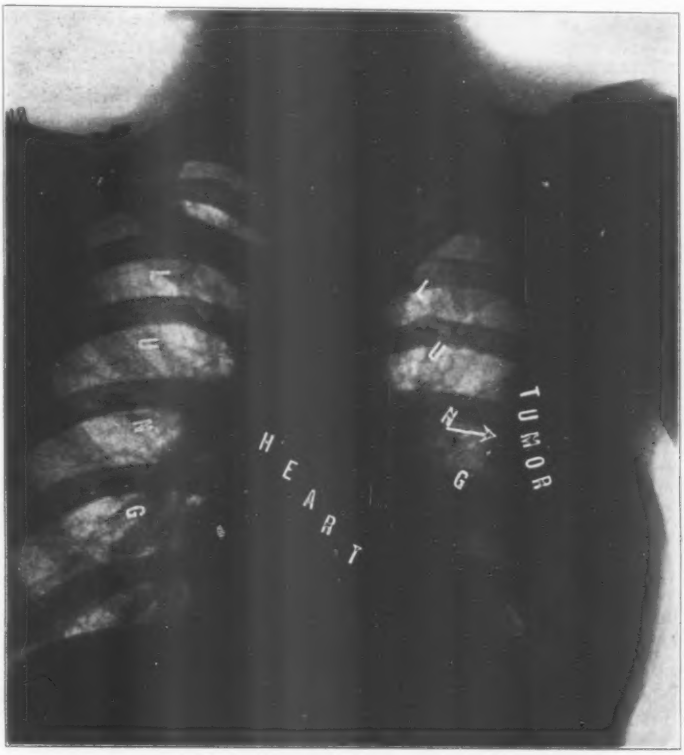


FIG. 4.—Embryonal carcinoma of left lung after treatment, May 14, 1915.

THERAPEUTIC RESULTS BASED ON PHYSIOLOGICAL ACTION OF THE ROENTGEN RAYS. The improvements obtained in certain classes of cases are such as might be expected when one considers the physiological action of the roentgen ray.[1 22] It has been shown that the deep tissues of the body which are most susceptible to roentgen rays are the lymphoid tissues of the spleen, lymph glands and follicles, thymus gland, the spermatogenous epithelium of the testis, the Graafian follicles of the ovary, endothelial cells, embryonal cells, and the nucleus of cells, especially those in an active state of division.

Based on these physiological actions it is logical to expect that we would find the greatest therapeutic effects of the roentgen rays in diseases causing lymphatic, testicular, and ovarian tumors and tumors made up of embryonal cells, and this is borne out in experience as we get most effect in lymphosarcoma, the leukemias, embryonal carcinoma, carcinoma testis of teratoid origin, and adenocarcinoma of the ovary. In this series of cases we were fortunate in being able to observe 33 cases of lymphosarcoma and 18 cases of Hodgkin's disease. These cases will be published in detail subsequently.

CONCLUSIONS. From a study of these cases we are justified in drawing the following conclusions in regard to the value of roentgen rays in cancer:

1. Roentgen rays give excellent therapeutic results in basal-cell epithelioma.

2. They ameliorate cases of carcinoma of the breast, ovary, and testis, tumors lymphatic structures especially when these tumors are made up of cells of an embryonal type.

3. While we cannot successfully maintain that the roentgen rays have yet proved to be a cure in cancer it is worthy of note that these rays as well as those of radium applied with removal when possible produce more uniform improvements in cancer than any other agents heretofore known, and the use of these agents in cancer is established until some effectual constitutional treatment for cancer is found.

4. Pending the discovery of some effectual constitutional treatment every effort should be made to increase the ameliorating effects of the radio-active methods.

5. Surgery should not ignore the benefits of these methods in the treatment of cancer, particularly in the postoperative raying and treatment against metastases.

6. Most of our improved cases eventually relapsed, and while their lives were prolonged and made more comfortable by the roentgen-ray treatment they eventually died of the disease.

7. In some instances these ameliorating effects were very striking and deserve particular attention in the hope that we may eventually discover means of making these ameliorations more lasting and even permanent.

CASE HISTORIES. *Results of Deep Roentgen-ray Treatments in 258 Cases of Malignant Tumors.*

CASE II.—Mrs. Mc. K.; aged forty-five years.

Microscopic Diagnosis. Alveolar carcinoma breast.

Chief Complaint. Recurrent tumors of breast and enlarged glands above the clavicle.

Family History. One grandparent, mother, and one sister had cancers.

Personal History. Patient was operated on for ectopic gestation in 1907. Had a hysterectomy for myoma in 1910.

Present Illness. Onset in November, 1913, with the appearance of two nodules in the right breast. No pain. Nutrition good.

December, 1912. Radical amputation of right breast and dissection of axillary glands. (Dr. C. H. Peck, Roosevelt Hospital.)

Pathological Report. "Section of the tumor mass is composed entirely of epithelial cells, packed away together and lobulated, with dense fibrous connective-tissue bands containing numerous small round cells, a few polynuclears, moderately congested bloodvessels, and some fat. The fibrous stroma is slight, the cellular elements predominating. Mitoses are present. Section of the smaller mass shows groups of these cells having the same characteristics invading the breast tissue. Section from the axillary glands shows a thickened capsule and trabeculæ rather densely infiltrated with small round cells and containing a few congested bloodvessels, and the lymphoid tissue is almost entirely replaced by invading groups of epithelial cells having the same general characteristics as the original tumor. Mitoses are numerous." (Baldwin Mann, pathologist.)

Received postoperative roentgen-ray treatments for one month.

March, 1913. Recurrences developed along the healed scar. Enlarged glands appeared above the clavicle and in the epigastric region.

November 10. Massive deep roentgen therapy begun, treatments being administered to all sides of the chest, axillæ, and neck. 510 X (Kienboch) units being administered with water-cooled tubes and 1290 X (Kienboch) units being administered with Coolidge tubes. Total 1800 X (Kienboch) units. One persistent nodule in the scar about 4 cm. long was treated with radium, total 98 millecurie hours (Dr. H. H. Janeway) filtered through 1 mm. of lead administered in eight treatments. Under this treatment all nodules disappeared and the patient was symptom-free until October 20, 1915 (a period of nearly two years). At this time she complained of pain in her back (lumbar region). Roentgen-ray examination showed no evidence of bone metastases. The pain was very much relieved by roentgen treatments.

December, 1915. Patient developed general metastases all over her body. Large masses appeared in the left breast, which was enormous and had a hog-skin appearance. The left axilla was involved. Pain developed in chest and back. The patient was evidently progressing into a stage of general carcinosis. On account of the fact that the gamma rays of radium are more penetrating than the hardest roentgen rays generated from a Coolidge tube it was decided to use large quantities of radium emanations, heavily filtered, under Dr. H. H. Janeway's direction. Between January, 1915, and July, 1916, she received a total of 51,908 millecurie hours of radium, using distance and various metal filters. Under this treatment the tumors diminished very greatly in size and changed from edematous swollen masses to hard contracted masses. The left breast became adherent

to the chest wall. The patient's symptoms were greatly improved for a time; later she gradually failed, but is still alive at the present time.

The important points in this case are the strong family history of cancer; the well-developed and excellent nutrition of the patient, the development of a malignant type of cancer of the breast, as shown by its clinical course and morphology. The radical operation within one month of the appearance of the tumor by a very competent surgeon under ideal hospital conditions; the recurrence of the growth with palpable supraclavicular and epigastric metastases within four months after the operation, rendering her in a condition hopeless for further operative intervention; complete relief of symptoms and palpable evidences of disease under roentgen-ray and radium treatment for two years subsequent to the development of this hopeless condition; after which she developed a condition of carcinosis which was ameliorated by enormous doses of radium emanation. The analgesic and alterative actions of roentgen rays and radium. The patient is still alive four years subsequent to the onset of her original disease and three years eight months after the development of hopeless metastases.

CASE III.—C. S., male; aged forty years.

Microscopic Diagnosis. Lymphosarcoma.

Chief Complaint. Recurrence of tumor of face on the left side.

Duration. Ten years.

Family and Personal History. Negative.

Present Illness. Began ten years ago with the appearance of a nodule on left side of face close to the ear. He was operated on several times. A year ago the patient was treated with mixed toxins. The tumor retrogressed. The patient continued to be treated with toxins while at home, but with no permanent improvement.

Physical Examination. The patient is a well-nourished man in middle adult life, who has a tumor of the left side of the face. His jaw is limited in motion, so that the teeth can only be parted one-third inch. His tonsils and pharynx we were unable to examine. There is facial paralysis of the left side of the face. The region of the left ear and all its surroundings show a hard prominence, which is red, and especially so behind the ear. The external canal of the ear presents an ulcerated area covered with a purulent discharge. The scars of previous operations are seen beginning from the lobe of the ear and ending about $3\frac{1}{2}$ inches below. The lymph nodes are not enlarged. The abdomen is soft and no masses felt. No edema of the legs. Patient had been under treatment with mixed toxins for a period of about two years, but the growth did not diminish any so it was then decided to add roentgen-ray treatments.

November 20, 1913. Roentgen-ray treatments were begun, and in all he received seven massive treatments. After the third treatment (December 15) the tumor began to retrogress very markedly

and by the end of January, 1914, the entire mass was gone. Patient left the hospital in a fairly good condition. The growth did not recur. The patient died six months later from nephritis.

Carcinoma Testis of Teratoid Origin. This class of cases also gives us uniform initial improvement, followed by ultimate relapses. In our series we had 5 cases; all improved; all died.

CASE IV.—Male; aged twenty-nine years.

Microscopic Diagnosis. Carcinoma testis of teratoid origin with abdominal metastases.

Chief Complaint. Tumors in abdomen particularly in the splenic region.

Personal and Family History. Negative.

February, 1914, he first noticed an enlargement of the left testicle. In March this tumor was removed and the patient was symptom-free until July, when he had a sudden onset of abdominal pain, and on examination a tumor mass was discovered in the left lower abdominal quadrant. The patient was then treated until March, 1915, by Dr. J. W. Vaughn's (Detroit) serum method, under which the tumor grew smaller for a time, but subsequently relapsed.

Physical Examination. A well-nourished young man with no evidence of poor health except a hard mass in the left side of the epigastrium about the size of an orange. Its outline is regular and it lies for the most part under the left rectus muscle. It is not tender on deep palpation. Liver is not enlarged. No ascites. Lymph nodes in groin slightly enlarged. Wassermann reaction negative. He was placed on several special treatments by Dr. S. P. Beebe, without any apparent change in the patient's condition.

March 19 he was given a treatment over the abdominal tumor, after which it was noticeably diminished in size. The treatments were repeated over the enlarged glands in the groin, after which they disappeared. The special treatments were continued and the roentgen-ray treatments stopped, followed by prompt recurrences of the enlarged glands in the groin. Roentgen-ray treatments were resumed at the patient's request and the tumors again disappeared.

May 29. Roentgen-ray examination of the chest showed metastases in the hila of both lungs. The patient received a total of 21 massive roentgen treatments over the abdominal, inguinal, and mediastinal lymph nodes. These enlargements were all reduced under this treatment and were held in abeyance up to July, when the patient discontinued treatment. The tumor masses subsequently recurred and the patient died of exhaustion.

Summary. Case of carcinoma testis of teratoid origin. Primary tumor removed within a month of the onset. Metastases developed within four months after operation. The generalized metastases were treated eight months by Vaughn's serum method, with primary improvement and subsequent relapse, he was then treated by a combination of special treatments, including autolysin and roentgen-

ray treatments covering a period of five months; it was noticeable that the size of the tumor diminished after each roentgen-ray treatment and at times were made to disappear and when the roentgen rays were omitted the tumors promptly reappeared; it is therefore logical to assume that the ameliorations were due directly to the roentgen-ray treatments. The patient subsequently died of exhaustion. This was the first case of this class of tumor which we had treated and before we knew of the efficacy of roentgen rays.

CASE V.—E. W.: female; aged seventeen years. Admitted to Memorial Hospital, January 10, 1915.

Chief Complaint. Swelling on the left side of the chest. Shortness of breath.

Present History. Six months ago (July, 1914) the patient began to have sharp pains around her heart, in the left axilla, and in her back. The pain lasted only a few seconds at a time. About the same time she became short of breath. She could not walk a block without resting two or three times. Six weeks ago she first noticed a small swelling near the left axilla. The swelling has increased in size very little since she first noticed it. Now she occasionally has pain in the swelling in her back. She has had several night-sweats. No cough. Has expectorated a small amount of whitish material. Nose bleeds occasionally. December 26 she was tapped, 1500 c.c. of fluid being obtained. She was admitted to the Jewish Hospital two weeks ago and was tapped again one week ago, 1500 c.c. being obtained.

Past History. Two years ago she had a cough which lasted a month.

Family History. Negative.

Physical Examination. The patient is a moderately well-developed and well-nourished girl, aged seventeen years. Mucous membranes rather pale. Skin normal. On the left side of the thorax, in the anterior axillary line, just below the lower edge of the pectoralis major muscle and partially covered by that muscle, there is a hard mass 10 cm. in diameter. The mass is circular in shape, has a smooth surface, and is firmly fixed to the chest wall. Skin over the mass normal in appearance and movable. Left chest appears larger than the right. Intercostal spaces on the left side bulging. Left chest immobile on respiration. Right chest moves normally.

Palpation. Tactile fremitus present on the right side and absent on the left side.

Percussion. Flatness over the whole left chest, both anterior and posterior. Normal resonance on right side.

Auscultation. Breath sounds distant over the whole left chest. Somewhat tubular in character in the lower part. On the right side breath sounds are normal. No rales or friction sounds heard.

Heart. Apex beat cannot be seen or palpated. On percussion the cardiac dulness extends one inch to the right of the sternum. Left

border of heart not made out. Heart sounds indistinct, except at the right border of the sternum. Regular and of good quality. Pulse rate 90 and of good force.

Abdomen. No masses, tenderness, or rigidity. Liver cannot be palpated. On percussion the liver dulness extends almost to the umbilicus. Spleen and kidneys cannot be palpated.

Summary. A moderately well-nourished girl, aged seventeen years. Hard, movable tumor, on anterior chest wall at the lower border of the left pectoralis major muscle. Flatness over the whole left chest with distant breath sounds. Heart displaced to the right. Liver enlarged. Palpable lymph nodes in groins. Roentgen-ray examination shows that the entire left side of the thorax is filled with a mass of tumor tissue with some effusion. Chest aspirated. 1000 c.c. of bloody fluid obtained. Tissue was removed under local anesthesia, on which the following pathological report was made:

"Tumor of axilla. The tumor is a malignant growth composed of small round and polyhedral cells. The structure is peculiar. There are many small arterioles with thickened or hyaline walls to which are attached the small tumor cells, as in perithelioma. Between these units are diffuse masses of tumor cells. The tumor cells resemble lymphocytes, but show a polyhedral tendency which suggests an epithelial or endothelial origin. There are many mitoses. The tumor may be a lymphosarcoma, or a malignant embryonal growth from some glandular organ."

Massive roentgen-ray treatments were begun, followed by noticeable improvement within ten days. The treatments were continued and the external tumor disappeared. Roentgen-ray examination showed pronounced diminution in the size of the intrathoracic tumor. Heart returned to its normal position. Lung relations on the right side have resumed their normal place. Patient discharged to the out-patient department February 27.

Condition. General health has improved. She has gained weight during the past three weeks. Still complains of sharp pains in the lower part of the left chest.

Physical Examination. Mass in left axilla almost disappeared. Moderate resonance over anterior and posterior part of left chest. Impaired resonance in left axilla and at base of lung. Breath sounds normal except over the dull areas where they are not heard distinctly. No rales or friction sounds heard. Heart seems to be in normal condition. Patient's condition continued to improve and she became symptom-free, remaining so until September 10, when she was readmitted because of shortness of breath. Roentgen-ray examination of the chest showed the tumor growing rapidly. Her general condition became gradually weaker and dulness developed over the entire left chest. Cardiac impulse displaced to right of sternum in the third interspace. Abdomen distended and tympan-

itic, and there was apparent paralysis of both legs. November 13 the patient died. No autopsy was permitted.

Summary: Duration: Fourteen months previous to treatment. Microscopic diagnosis: embryonal carcinoma of the chest of unknown origin. (A type of tumor which is unique in medical literature.) A large tumor mass almost filled the left chest. A hard movable tumor mass presented on chest wall. No metastases demonstrable. Marked dyspnea. Patient received 28 massive roentgen treatments (840X) between January 22, 1915, and August 1, 1915, during which time she became symptom-free and much improved in health The external tumor disappeared; the intrathoracic tumor diminished as shown in the illustrations. One month later the patient's symptoms suddenly returned and progressed despite all forms of treatment. Patient died of exhaustion.

BIBLIOGRAPHY.

1. Heineke: Mitteilung aus den Grenzgebieten der Medicin und Chirurgie xiv, 1905.
2. Menetrier and Touraine: Arch. d. mal. du coeur, 1910, iii, pp. 641–663.
3. Heineke: München med. Wchnschr., 1903–1904.
4. Rudberg: Arch. f. Anat. u. Physiol., 1907, Anat. Abtg. Supp., p. 123.
5. Aubertin et Bordet: Centralbl. f. micro. Medizin, 1909.
6. Pigache et Beclere: Ref. Ztschr. f. Röntgenk., 1913, xv, p. 2. (Bulletin de la Soc. anatomique, 1911).
7. Regand et Cremien: C. R. Soc. de biol., 1911–1912, lxxii, p. 523. (Arch. d'Elect. Méd., 1912, xx, p. 481; 1912, xxi, pp. 144, 597).
8. Eggers: Ztschr. f. Röntgenk., 1913, xv, pp. 1, 44.
9. Bergonie et Tribondeau: Arch. d'Elect. Méd., xiii, pp. 149, 474 et seq.; C. R. Soc. biol., 1904, v, p. 400 et seq.; ibid., December 10, 1906.
10. Halberstadter: Berl. klin. Wchnschr., No. 3, 1905.
11. Bergonie: Tribondeau and Recamier, Comp. rend. Soc. de biol., 1905, ibid., p. 284.
12. Roulier: Compt. rend. Soc. de biol., August, 1906.
13. Specht: Arch. de Gynäkol., 1906, lxxviii, Heft 3.
14. Okintschitz: Ref. Ztschr. f. Röntgenk., 1910, xii, p. 236.
15. Saretzky: Ref. Ztschr. f. Röntgenk., 1910, xii, p. 235.
16. Langfellner: München. med. Wchnschr., 1906. No. 44.
17. Fraenkel: Centralbl. f. Gynäkol., 1907, No. 31.
18. Krause and Zeigler: Fortschr. a. d. Geb. d. Röntgenstr., vol. x.
19. Reifferschied: Ztschr. f. Röntgenk., 1910, 1e, p. 232.
20. Simon: Ztschr. f. Röntgenk., 1911, xiii, p. 371.
21. Gassman: Fortschr. a. d. Geb. d. Röntgenstr., 1899, xi, p. 197.
22. Leon: Cong. d. dent. dermat. Gesellsch., 1901.

SYPHILITIC AORTITIS.[1]

By Arthur R. Elliott, M.D.,
CHICAGO.

(From the Medical Service of St. Luke's Hospital, Chicago.)

The development of internal lesions in latent syphilis is attended by such vague indefinite clinical manifestations as to render diagnosis

[1] Read before the Chicago Society of Internal Medicine, February 28, 1916.

during their incipiency often a matter of extreme difficulty. This obscurity of early signs and symptoms characterizes aortitis, and previous to the introduction of the Wassermann test and the employment of roentgen diagnostic technic, the lesion usually came to light only when it had advanced to the production of gross and often obvious mechanical manifestations. On account of its usual prolonged latency it was described according to the classification formerly in vogue as a form of so-called parasyphilis, the occasional case that pursued an active rapid course hardly sufficing to disturb this rating. As a parasyphilitic manifestation, aortic syphilis remained more or less separated in interest from the parent disease, and the role assigned to it being that of a late nutritive secondary it was viewed with comparative indifference. The isolation of spirochetes in the tunics of diseased aortæ and accumulated studies with the Wassermann test have in recent years combined to endow aortic syphilis with new significance, revealing the lesion in its proper light as true syphilis subject to all the activities and amenable to the same therapeutic attack as other forms of internal syphilis. Although pathologists describe fairly acute inflammatory changes at the root of the aorta in certain acute infections, notably rheumatism, these occur almost always in association with endocarditis, and, moreover, manifest a tendency to spontaneous subsidence very different from the progressive character of the aortitis of syphilis. These transitory non-specific types of aortitis are very little familiar to the clinician, so much so that it may be said, speaking clinically, there is but one form of aortitis, the syphilitic.

The Wassermann test has materially altered our views regarding the specific nature of aortic lesions. A positive Wassermann reaction has been obtained in over 80 per cent. of cases that showed characteristic aortic changes at autopsy, Eich's statistics showing 81.8 per cent. and Pearce's 78.5 per cent. Citron used the Wassermann test in all chronic cases of aortic regurgitation and found it positive in 60 per cent. Collins and Sachs tested 13 cases of aortic valvular disease finding the Wassermann positive in 11. By way of contrast they record an equal number of cases of purely mitral disease, similarly tested, with Wassermann positive in but 2 instances. Still more direct evidence of the syphilitic nature of aortic disease has been furnished by the isolation of the spirochete of syphilis in the tunics of diseased aortæ, such a finding being now of common occurrence. Moreover, the fact that lesions practically the same as syphilitic aortitis in the acquired disease have been found to exist in a high percentage of infants with congenital syphilis affords strong support to the claim that the lesion in adults is due to syphilis.

Syphilitic aortitis before it involves the valves is often latent. After it has produced aortic valve incompetency its progress is rapid, often bringing life to an end within two or three years.

Aortic regurgitations of syphilitic origin do very badly probably because of the association of deformed valves and constricted coronary orifices. The prognosis is far more serious than in cases of rheumatic origin even when of equal degree, compensation being less well established and the aorta more dilated.

Early in the course of aortic syphilis the involvement of a limited portion of the artery may appear of slight immediate significance. Its progression involves the risk of serious damage with, it may be, dilatation or aneurysm angina pectoris or most commonly aortic regurgitation. To detect this insidious lesion before it has advanced to the production of mechanical secondaries is consequently of great importance. Clinical recognition of the disease in its earliest stages gains greatly in importance from the fact that it may be treated by intensive antisyphilitic methods with some prospect of control. The diagnosis is often extremely difficult, since limited and circumscribed changes in the ascending portion of the aorta without involvement of the valve ring are seldom accompanied by clearly defined symptoms or signs. The greatest difficulty is encountered in individuals not recognized as being syphilitic. It is often the case for aortitis to be the only manifestation of the disease in otherwise latent syphilis, and one may expect in a considerable percentage of cases to encounter a completely negative history of syphilis. In one-half of Benary's cases and in 28.9 per cent. of Symmer's autopsy material, aortitis was the only manifestation of the disease detected at autopsy. The majority of patients coming under clinical recognition for aortic syphilis are in middle life, and experienced clinicians understand the significance of angina pectoris and aortic regurgitation originating in the adult.

Our most valuable aids in the diagnosis of obscure aortic disease are the Wassermann test and roentgen-ray examination.

It is now generally conceded that a positive Wassermann reaction means active syphilis somewhere in the body. From the frequency with which syphilitic arotitis is found accidentally at autopsy (according to Eich 42.8 per cent. of cases) we may assume that the infection may be harbored in that part of the vascular system for years without detection; indeed, it might even appear that the aorta is one of the main situations in which the infection may lurk in latent syphilis. A persistent Wassermann reaction in an otherwise latent case may consequently direct suspicion toward the aorta and a roentgen-ray study of this area should be made. The absence of a definite or confessed history of syphilitic infection should not be allowed to divert attention from such a possibility. This is especially important in women in whom historical data on this point are, for obvious reasons, obscure and unreliable. A negative blood Wassermann in a known syphilitic should not be accepted as inconsistent with a possible aortic lesion. Progressive aortitis may exist, although the blood has been Wassermann nega-

tive for years. The luetin test of Noguchi may occasionally reveal the disease when the Wassermann reaction is negative, as in certain cases presently to be related. Bearing in mind this frequency of aortitis in latent lues it is well that we should consider the possibility of a syphilitic etiology in any case of cardiovascular degeneration of obscure origin. If serological studies confirm this suspicion the aorta should be carefully examined by means of modern roentgen-ray technic.

The symptoms of syphilis of the aorta are pain in and about the precordium, dyspnea, hoarseness, paroxysmal cough, tachycardia, arrhythmia, general weakness and lassitude, and, under certain circumstances, elevated blood-pressure. These symptoms are seldom clearly defined during the period of early development of the disease. Various clinical criteria, such as the shape of the heart to percussion, peculiarities of rhythm, the paroxysmal nature of cardiac symptoms have been proposed to identify syphilitic aortitis. One need not emphasize the unreliability of such data.

There are certain physical signs which may be elicited by examination in most well-developed cases, but they are not of such a character as to especially indicate aortic syphilis. Among the most significant of these signs are a roughening or impurity of the first aortic sound and a sharp ringing aortic second tone, which if the aorta is much dilated may have a bell-like quality. Extension upward of percussion dulness over the sternum may exist, and there may be abnormal pulsation in the carotids and subclavian with an impulse in the episternal notch. None of these signs are, however, sufficiently characteristic to furnish grounds for diagnosis of syphilitic aortitis, since they are frequently noted in aortic atheroma and high blood-pressure states not connected with syphilis.

The primary aortic involvement is a small cell or granulomatous infiltration of the tunica media (mesaortitis) along the course of the vasovasorum. Eventually all three of the main coats of the aorta become affected the intima by secondary proliferative thickening. Coagulation necrosis, and subsequent connective-tissue changes lead to slow but extensive damage to the vessel wall, so that fairly characteristic gross appearances become established. Although maximum involvement appears to fall upon the first part of the arch and the ascending aorta probably because of the greater functional strain to which this portion of the vessel is subjected, no section throughout the vessel is exempt from attack. The involved areas appear as more or less well-defined elevated patches, the surface of the larger areas being often extremely irregular, with pittings, scars, and puckerings, making what Allbutt describes as "knotty masses" in the vessel wall (Fig. 1).

When secondary changes are extensive they are characterized not by calcification, as in arteriosclerosis, but by a gradual corrosion or thinning by scar formation, so that the vessel wall may become

translucent at points and there may be tiny aneurysmal bulgings or possibly a true saccular aneurysm. Frequently cellular infiltration about the mouths of the branches of the arch may cause distinct narrowing of innominate and left carotid or more or less occlusion of the coronaries.

In the earlier stages the vessel is perhaps but little dilated or deformed. If viewed from without little change may be noted (Fig. 2). It is on the inner surface of the artery that the changes appear (Fig. 3). The tendency of the disease in development is to spread to the aortic valve and by a general periarteritis in the cusps and between them the semilunar valve flaps become thickened and deformed, giving rise to valve incompetency. It is a common

FIG. 1.—Syphilitic aortitis with diffusely dilated vessel. (From Pathological Museum, Rush Medical College.)

and important clinical observation that the aorta may be gravely affected, although the peripheral arteries apparently remain normal, and Brooks has emphasized the fact that the coronaries are apt to show a degree of involvement out of all proportion to general arterial change. It is the seat of the disease in the suprasigmoid portion of the aortic arch that threatens the integrity of the coronaries, and the steady progression of the disease accounts for the aortic valve defects aneurysm and anginas which constitute the morbid end-products of syphilitic aortitis.

Of all the methods of diagnosis to determine the presence of aortic disease, the roentgen ray is the most valuable. By its aid we may detect slight changes in the caliber and shape of the vessel

which entirely elude the methods of physical examination. Both fluoroscopic inspection and plate studies should be employed, the

FIG. 2.—Syphilitic aortitis, outer surface of vessel.

FIG. 3.—Syphilitic aortitis; inner surface of vessel. (From Pathological Museum of Rush Medical College.)

former for preliminary observation and the detection of abnormal pulsation and the latter to secure definite outlines and measurements.

The various roentgen-ray plates herewith reproduced were taken in the standing position, with a few seconds' exposure, and focal distance of seven feet, which provides for practically parallel rays and obviates distortion of the shadow.

The shadow of the normal aorta in the roentgenogram (Fig. 4) lies in its first portion behind the sternum and does not project beyond the right auricular curve. At the arch where it curves backward and to the left there appears a more or less well-rounded knob seen to the left of the sternum well above and distinct from the cardiac shadow. This aortic knob is not equally well defined in all normal aortæ. In the asthenic or dropped heart type it may hardly show at all, whereas in occasional cardiac roentgenograms it may be so prominent a feature as to be mistaken for aneurysmal bulging.

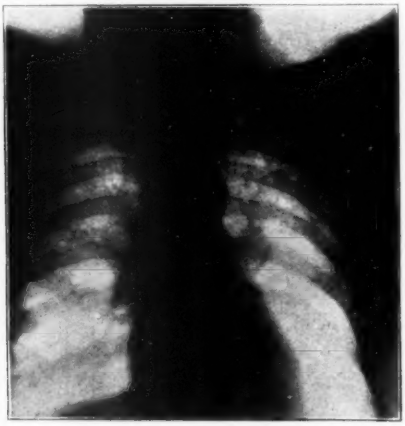


Fig. 4.—Normal aortic shadow.

It varies in prominence according to age, being less defined in early life than in adults, and in the aged and arteriosclerotic individuals the shadow may be sharply outlined and intensified from sclerous thickening and lime deposits (Fig. 5). It is less apt to be prominent in adult females than in males of corresponding age.

In aortitis the roentgen ray reveals two kinds of changes, *i. e.*, alterations in density of shadow and changes in contour. In early aortitis the pathological process is almost invariably confined to the very origin of the aorta. As the vessel is not at this stage thickened and no lime deposits exist there may be merely a slight dilatation of the first part of the arch with exaggerated pulsation at that point. Wessler points out that some dilatation of the aorta is a very common finding in routine cardiac roentgenography, so that little special significance attaches to it. It is practically con-

stant in ordinary sclerosis of the aorta and in high blood-pressure states. In non-specific aortic sclerosis, however, it is nearly always accompanied by a prominence of the whole arch, and if blood-pressure be elevated by hypertrophy of the left ventricle.

In early cases of aortitis the heart is rarely enlarged unless there is coexisting valve defect or hypertension. Of course, aortitis and atheroma may be combined in the same case, when computation will be rendered difficult. With the progress of aortitis the artery becomes more and more dilated, and, as a result, the aortic shadow as it ascends from the heart is widened so that it projects beyond the shadow of the curved right auricle. In most instances the shadow is regular, but it may show slight bulgings or protrusion.

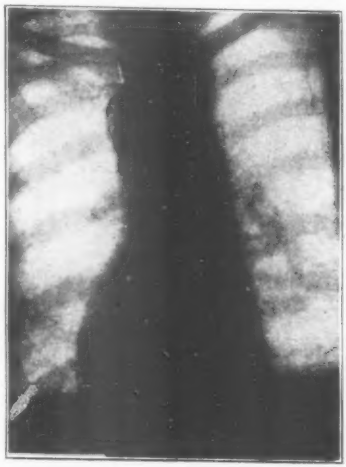


FIG. 5.—Non-specific aortic sclerosis. Note lime deposits at aortic knob.

Should the aortic dilatation extend to the arch the knob as it curves to the left may lose its well-defined curve, becoming flattened and broadened. Longcope has described a type of case in which the aortic shadow appears as a more or less truncated cone, with rounded apex and broad base resting on and fusing with the cardiac shadow. In any well-developed instance there may appear above the aortic shadow a pyramid-shaped shadow with base upward and beneath the clavicles. This seems to represent the dilated great arteries as they arise from the arch (Fig. 6).

While in the earlier stages of aortitis roentgen evidence may consist merely of a slightly increased curvature and pulsation at the aortic ampulla, a gradual dilatation and lengthening of the vessel supervene with further progress of the disease. These changes

combine to broaden and elevate the aortic shadow, and there occurs in most cases some enlargement in the size of the heart whether

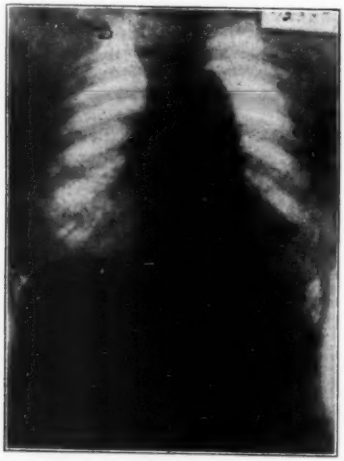


FIG. 6.—Advanced syphilitic aortitis with aortic valve insufficiency. Marked dilatation of aortic arch and great vessels as they arise from arch.

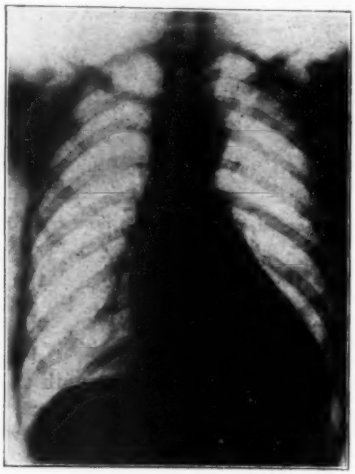


FIG. 7.—Non-syphilitic aortic insufficiency illustrating "aortic configuration" of heart shadow

aortic insufficiency be present or not. The increase in cardiac diameters affects to a much greater degree the long diameter than

the broad diameter of the heart, the organ assuming a position more nearly horizontal than normal, producing a heart shadow somewhat boot-shaped, the heart lying low on the diaphragm. This type of heart shadow is very similar to that seen in high blood-pressure states (nephritis), although the marked pulsation of the left ventricle seen in hypertension is less manifest. This type of heart might be termed the aortic heart (aortic configuration) (Fig. 7) in contradistinction to the broad, rather round, or bag-shaped heart of mitral disease ("mitral configuration") (Fig. 8). With the spread of the disease to the aortic valve and the production of aortic insufficiency we find the heart shadow much augmented and its horizontal configuration correspondingly magnified. In advanced cases with superadded relative mitral insufficiency both

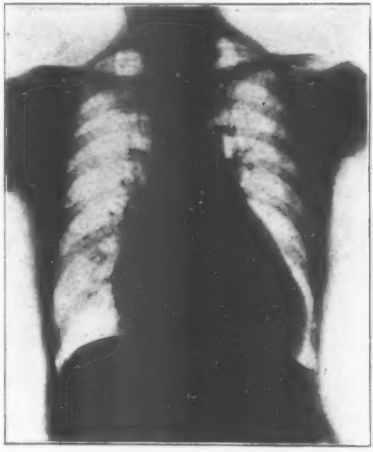


FIG. 8.—Mitral disease illustrating "mitral configuration" of heart shadow.

broad and long diameters are increased, combining to produce a very bulky heart shadow, the true cor bovis (Fig. 9).

It is obvious that until there is some dilatation, thickening, alteration of curve, or abnormal pulsation in the vessel, roentgen diagnosis of aortic disease is impossible. In consequence of this fact the roentgen ray cannot be relied upon for its detection in the early stage before mechanical defects begin to make their appearance. Clinical considerations and the Wassermann test must establish the diagnosis at this stage. An illustrative case may be cited.

CASE I.—A colored waiter, aged twenty-one years, complained of persistent aching pain in the left shoulder of two months' duration. This was accompanied by a recurrent substernal soreness, palpi-

tation, and a dry paroxysmal cough. He gave a history of chancre two years previous to consultation. On examination an appreciable enlargement of the heart could be made out, and along the left border of the sternum a faint diastolic whiff was heard. Firm pressure over the manubrium sterni caused a deep-seated aching soreness. Blood Wassermann positive. Blood-pressure systolic, 155; diastolic, 85; pulse-pressure, 70. The roentgen ray beyond some enlargement of the heart failed to reveal anything of significance.

The clinical diagnosis was manifestly aortitis of rather active type, yet at a stage too early for stretching of the aorta or other mechanical defect to appear upon the roentgen-ray plate.

FIG. 9.—Extreme cardiac effects of aortic syphilis, *i. e.*, aortic regurgitation, relative mitral insufficiency, pulmonary hypostasis. This patient is alive, two years after this plate was taken.

In contrast to this type of case may be cited the following instance in which the roentgen ray confirmed and established beyond doubt the clinical diagnosis.

CASE II.—A white man, aged forty years; widower; one child; complaint: hoarseness, cough on exertion, dyspnea. Acknowledges luetic infection ten years previous to consultation, for which he received almost continuous treatment for four years. Blood Wassermann, typically positive. Physical examination showed a somewhat enlarged heart, with a ringing second aortic tone. The pulse was regular. Blood-pressure: systolic, 140; diastolic, 100; pulse-pressure, 40.

The roentgenogram (Fig. 10) showed typical aortic configuration of the heart, with bulging of the first part of the ascending aorta,

The following example of well-developed syphilitic aortitis possesses points of unusual interest:

CASE III.—Single white man, aged forty years; complaint, palpitation and irregular heart action, lack of endurance, lassitude, and depression. Gave a history of lues at age of twenty-nine, with continuous treatment for two years. For three years previous to consultation blood Wassermann tests have been made at regular six-month intervals, with invariable negative reports. The last Wassermann test was taken six months before roentgenogram was made and proved negative.

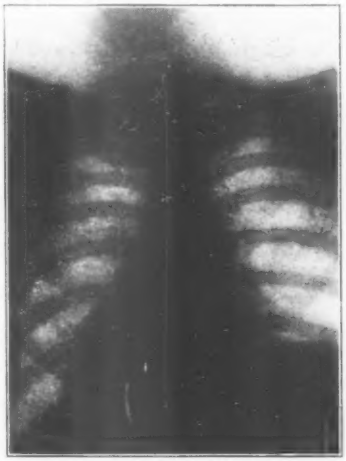


FIG. 10.—Case II. Heart shadow displays aortic configuration with bulging of first portion of ascending aorta.

Physical examination revealed an enlarged heart, aortic systolic murmur, accented second aortic tone, premature contraction arrhythmia. Blood-pressure: systolic, 210; diastolic, 150. Early tabetic signs. The urine contained albumin and casts. Renal function index with the 'phthalein test 60 per cent. Clinical diagnosis: syphilitic myocarditis, nephritis. The roentgenogram showed a typical aortic type of heart and stretched aorta.

The points of particular clinical interest in this case are the existence of extensive and probably progressive cardiovascular lesions of syphilitic type in an individual who for several years had been Wassermann negative, and was led to consider himself cured of his syphilis. The extent of damage already wrought by the cardiovascular disease would appear to indicate that it was of some years' standing.

The peculiar lassitude and depression which was the chief complaint of this patient is a symptom interpreted by Allbutt as significant of coronary involvement. A point of interest to be noted in this case is the association of aortic disease with signs of early tabes. This is an association frequently noted in the literature. In manifest tabes, Stadler found aortic disease in almost all cases. He regarded so-called cardiac crises as being in reality angina pectoris due to coronary stenosis. Strümpell emphasized the frequent association of aortic syphilis and tabes and statistics from various sources attest its frequence. In general, symptoms of aortic disease appear later than the earliest tabetic manifestations. This is perhaps not because aortitis is a later development but rather that it has a longer latency than tabes.

The cases thus far briefly described represent aortic disease in a relatively early stage of its development. Progress of the lesion inevitably tends to impair the integrity of the aortic valve producing as a result insufficiency of the valve apparatus. How soon this mechanical secondary comes to pass depends more upon the activity of the process than upon its duration. No estimate can be given of the average period required for the production of valvular defects, although, generally speaking, it is certainly not an early development. Occasionally valvular disease is seen to develop early and run a rapid fatal course, as in the following instance:

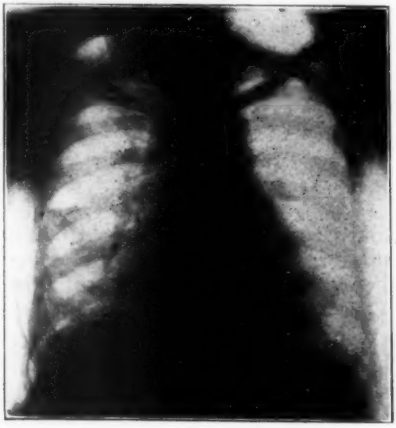


FIG. 11.—Case IV. Aortic and cardiac dilatation.

CASE IV.—Colored porter, aged twenty-five years; complaint, severe dyspnea, precordial pains. Duration of symptoms, six weeks; advent sudden; previous health considered good until development of foregoing symptoms. Luetic infection at age of

twenty; no active antisyphilitic treatment. Blood Wassermann strongly positive. Clinical diagnosis: aortic insufficiency, relative mitral insufficiency, pulmonary hypostasis. Termination, death after one week in hospital seven weeks after development of cardiac symptoms. Roentgenogram (Fig. 11) was taken eighteen hours before death and shows a greatly enlarged heart increased in both long and broad diameters. The aortic shadow is increased in breadth and elevated reaching as high as the sternoclavicular angle. This case illustrates how rapid may be the cardiac disorganization produced by aortitis, death resulting in this case five years after the initial syphilitic sore.

Aortic disease was formerly looked upon as a late development in syphilis. While, generally speaking, and especially in a clinical sense, this may perhaps be true, it is by no means always so. Along with other cases reported in recent contributions (Brooks, Longcope) the foregoing clinical history serves to discount the claim that aortic disease has a long latency and slow progression.

The following case represents an interesting variant of the usual clinical course of aortic disease:

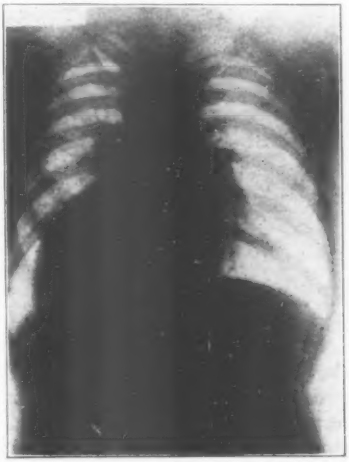


FIG. 12.—Case V. Anterior front view. Increase in both long and broad diameters; dilated aorta.

CASE V.—A white engineer, aged thirty-two years; married; two children, one healthy, one, dead at three weeks, "had a patent foramen ovale." Syphilis denied. Complaint: dyspnea, cough, tachycardia. Duration of symptoms three months; advent sudden, following exertion at high altitude. Urine contains albumin and casts. Renal function index, 50 per cent. Blood-pressure: systolic,

200; diastolic, 80; pulse-pressure, 120; blood Wassermann, strongly positive. Clinical diagnosis: aortic insufficiency, mitral insufficiency, nephritis. Roentgenogram (Fig. 12) shows the heart shadow increased in both length and breadth from the combined aortic and mitral incompetency. The shadow of the aorta is widened and rises high in the chest. Another semilateral roentgen exposure (Fig. 13) shows this well and indicates beautifully the enormous thickness of the heart shadow.

The duration of this patient's syphilis must rest on assumption and may perhaps be estimated as less than seven years (the age of his healthy child) and more than four (the date of birth of the congenitally defective child). The development of nephritis may by increasing aortic and cardiac strain have served to hasten the progress of the aortic disease.

FIG. 13.—Case V. Semilateral view.

CASE VI.—Colored cook, aged thirty-six years; complaint: dyspnea, chronic cough, orthopnea, slight edema. Duration of symptoms, six months. Previous health good. Syphilis denied. Blood Wassermann, strongly positive. Clinical diagnosis, aortic regurgitation. Roentgenogram showed aortic configuration increase in cardiac diameter 32 per cent. This case is a typical one of progressive syphilitic aortitis in latent syphilis and demonstrates how silent may be the progress of the vascular lesion until grave valvular secondaries arise. The liability of the colored race to cardiovascular syphilis is notorious and need not be emphasized here.

Syphilitic aortitis may exist in individuals who fail to react to the Wassermann test, as is shown in the following case:

CASE VII.—Hebrew peddler, aged forty-nine years; married; three children; complaint: pains in body, dyspnea, cough, general weakness. Duration of symptoms, one year. Syphilis denied. Blood and spinal fluid Wassermann negative. Luetin test typically positive. Roentgenogram (Fig. 14) shows heart to be of aortic configuration; *type asthenique;* dilated and lengthened aorta. Increase in cardiac diameter 10 per cent.

FIG. 14.—Case VII. Increase in cardiac diameter 10 per cent. Heart is of aortic configuration; asthenic or dropped heart type.

This with the following case illustrate that a negative Wassermann both blood and spinal fluid tests should not be taken as indubitably disproving a syphilitic etiology for aortic disease. The luetin test of Noguchi may reveal the disease and supply the necessary diagnostic link.

CASE VIII.—Colored housemaid, aged thirty-eight years; widow; complaint: orthopnea, chronic productive cough, no edema. Duration of dyspnea one week, cough chronic for three years. Syphilis denied. Blood and spinal fluid Wassermann both negative. Luetin test typical pustular reaction. Roentgenogram shows heart to be of aortic shape; costal-phrenic angle not clear on plate; dilated aorta. Increase of cardiac diameter 20 per cent.

During residence in hospital patient had six typical attacks of angina pectoris, the paroxysms being relieved by nitrites. Intensive treatment with neosalvarsan and mercury brought about great subjective improvement. Three months after leaving hospital there had been no recurrence of angina paroxysms.

The following 2 cases represent slightly different aspects of aortic syphilis. In both instances the activity of the disease appears to fall on the further distribution of the vessel. In the first of the

2 cases the transverse portion of the arch and in the second the abdominal aorta had borne the brunt of the disease with the formation of aneurysm in both instances.

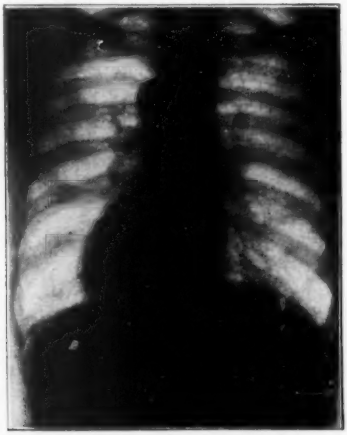


FIG. 15.—Case IX. Front view, showing prominent aortic knob only.

FIG. 16.—Case IX. Semilateral view, showing aneurysm of posterior aspect of aortic arch.

CASE IX.—Colored porter, aged thirty-four years; single; complaint: severe brassey unproductive cough, paroxysmal dyspnea, voice husky. Duration six months. Physical examination: slight tracheal tug, obscure systolic murmur at inner edge of left scapula just above its angle. Heart and chest otherwise negative. Left vocal cord paresis. Leutic infection at twenty-four. Blood Wasser-

mann strongly positive. Clinical diagnosis: aneurysm of thoracic aorta. Roentgenogram: the customary anterior-front view of the heart (Fig. 15) revealed a decided increase in the prominence of the aortic knob but the aortic and heart shadows otherwise were normal. As this somewhat obtrusive prominence of the knob is not rare in the normal aorta, and less rare in aortic atheroma, it could not be interpreted as of diagnostic value. An anterior semi-lateral view of the aortic shadow (Fig. 16) solved the problem, revealing a well-marked aneurysmal dilatation of posterior aspect of the aorta as it curves to the left and downward. This bulging could be seen rather indistinctly with the screen, but appeared much more clear-cut on the plate. The case furnishes a good example of the importance of screening all cases and of taking plates of more than one aspect of the aorta when doubt exists.

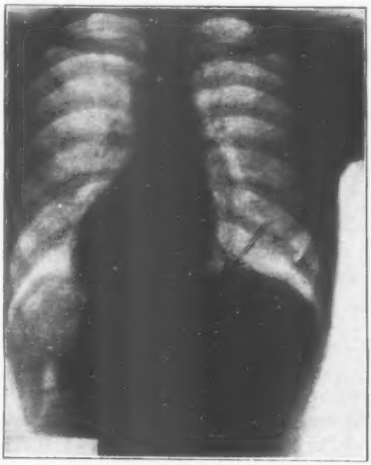


FIG. 17.—Case X. Note subcardiac shadow corresponding to abdominal aneurysm.

CASE X.—Colored porter, aged twenty-five years; complaint: pain in right hip; duration two weeks; previous health satisfactory. Physical examination revealed a plainly visible mass in epigastrium pulsating with expansile thrust synchronously with the heart's action. Luetic infection at sixteen. Blood Wassermann strongly positive.

Fluoroscopic examination, the stomach being distended with barium sulphate suspension, showed the stomach displaced to the left and pulsation of lesser curvature in contact with aneurysm.

Roentgenogram (Fig. 17) shows a practically normal heart and aortic shadow; below the heart is seen a dark shadow corresponding to the aneurysm.

The progress of the case was marked by gradual enlargement of the epigastric pulsating tumor and the formation of a large mass in the upper right abdomen, displacing the liver and right kidney downward and outward into the flank with the erosion of lower ribs posteriorly and the formation of a soft pulsating tumor in that region. Death occurred suddenly three months after admission.

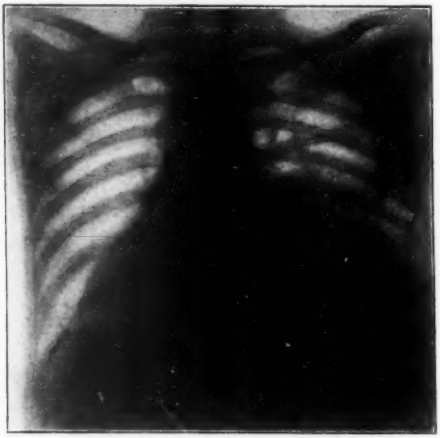


FIG. 18.—Case X. Roentgenogram taken just before death. Note displacement of right diaphragm with compression of right lung and displacement of heart upward. Aorta dilated.

Autopsy: Ventral saccular aneurysm of the abdominal aorta with the formation of a large false aneurysm, which contains organized blood clot weighing 990 grams. This false aneurysm is adherent to the diaphragm and right lower lobe of lung and to the eroded ribs and vertebræ. It extends down as far as the right psoas muscle. This mass is ruptured through the diaphragm near the aortic opening into the right pleural sac. A second roentgenogram (Fig. 18) was taken shortly before the patient's death. A comparison of the two roentgenograms will reveal a considerable contrast in heart contour. Upon admission the cardiac sounds were clear and heart outlines little different from normal. Toward the termination of the case the diastolic murmur of aortic insufficiency became plainly audible and the cardiac diameters increased. It is interesting to record that at autopsy no defect of the aortic valve cusps was apparent, but that the aortic ring was obviously dilated. Reference may be found in the literature to the fact that although the physical signs of aortic regurgitation exists during life, at necropsy the valves may appear surprisingly normal, regurgitation apparently depending upon dilatation of the aortic ring.

CONGENITAL ABSENCE OF LUNG.*

By A. G. Ellis, M.D.,
PHILADELPHIA.

(From the Laboratories of the Philadelphia General and Jefferson Medical College Hospitals.)

Complete absence of one lung is a rare condition. Theremin[1] found only two cases among 30,000 autopsies in a foundling asylum in Petrograd. Including those cases in which a tiny mass of cellular or possibly rudimentary lung tissue capped a short bronchus, I have found references in literature to 18 of what appear to be certain cases of absence of one lung. In addition there are at least 5 to be classed as possible cases, but remaining doubtful because of insufficient description. The 18 cases are briefly as follows:

1. Haberlein:[1] Soldier, aged twenty-four years. Right lung absent. No right bronchus. Right side of thorax filled by watery fluid. Left lung large; both bronchi enter it. Pulmonary artery enters undivided into left lung.

2. Haberlein:[2] Soldier, aged twenty years. Left lung absent. No left bronchus. No left pulmonary vessels. Left side of thorax filled by watery fluid. Right lung normal size, not diseased.

3. Hein:[3] Boy, aged six weeks, cyanotic. Right lung absent. Rudiment of right bronchus. Right pulmonary artery and veins absent. Defect in ventricular septum, open foramen ovale. Pulmonary artery closed at base of heart, left lung supplied by ductus arteriosus.

4. Stein:[4] Infant, aged six weeks. Right lung and pulmonary vessels completely absent. Rudiment of right bronchus.

5. Bell:[5] Young man. Left lung absent. Left pleural cavity filled by odorless fluid.

6. Maschka:[6] Child aborted at seven months; lived two hours. Right lung absent, heart in right side of thorax. Bronchus represented by pea-sized sac. Pulmonary artery and veins entirely absent. Left lung not lobed, otherwise normal. Esophagus ended blind at midpoint. Atresia ani.

7. Gruber:[7] Girl, stillborn. Right lung absent. No right primary bronchus. Right pulmonary artery and veins absent. Heart normal. Left lung no lobes, one pulmonary vein.

8. Herrero:[8] Man, aged sixty-five to seventy years. Left lung absent. Undivided trachea continuous with right bronchus. Right lung of enormous size.

9. Theremin:[1] Girl of eleven days. Left lung absent. Trachea continuous with right bronchus. A small hemispherical cartilagi-

* Read before the American Association of Pathologists and Bacteriologists, May 11, 1916.

nous nodule at site of left bronchus. Right lung no lobulation. No pulmonary veins into left auricle; they unite to form large vessel (1 cm.) that communicates with distended vena azygos. No deformity of chest. During life bronchial souffle and subcrepitant rales heard over both sides thorax posteriorly.

10. Theremin:[1] Girl, aged one hundred and twenty-seven days. Left lung absent. Trachea continuous with right bronchus. Cartilaginous elevation size of a pea at site of left bronchus. Left pulmonary artery and veins absent. Right lung imperfectly separated into two unequal lobes. Left auricle no veins, vein from right lung emptied into vena azygos. During life vesicular breathing heard on left side.

11. Gruber:[9] Female fetus; premature birth; did not breathe. Left lung absent. Trachea divided into three branches in hilum of right lung. Right lung not lobed. Pulmonary artery divided into right branch and ductus arteriosus. Heart normal, except only one vein into left auricle (came from lung in two branches).

12. Miller:[10] Male, aged four weeks. Left lung size of a pea, hanging on a thin bronchus. Pneumonia of right lung.

13. Miller:[10] Male, aged six weeks. Left lung size of cherry, hanging on a narrow bronchus.

14. Miller:[10] Female, aged two days. Left lung a mass of tissue 2 cm. in diameter, attached to narrow bronchus.

15. Tichomiroff:[11] Woman, aged twenty-four years. Died of pneumonia. Left lung absent. No primary bronchus. Trachea divided into three bronchi just before entering right lung. Heart normal.

16. Hanson:[12] Female child, full term, lived fifteen minutes. Left lung absent. Bronchus one-twelfth inch long, mass on end size of buckshot. Right lung rather smaller than usual. Heart on right side. Diaphragm lacking on left side with lower portion of small intestine and part of colon in left pleural cavity; appendix just beneath clavicle.

17. Findlayson:[13] Child lived some hours after birth. Right lung absent. Trachea ended in left bronchus. Pulmonary artery and veins undeveloped. Left lung hypertrophied, pushing heart to right.

18. Gross:[14] Boy, aged five months, twenty-three days. Left lung absent. Left bronchus 1 cm. long; blind; end rounded. Left pulmonary artery and veins absent. Heart normal. Right lung filled right thorax, mediastinum, and small part of left thorax; no definite lobulation. Thorax symmetrical. Other lesions included left-sided hypoplasia of face, dermoid of left eye, anomalous right renal artery, and atresia ani.

Doubtful cases of absence of one lung are those of Sömmering, Riviere, Pozzi, Heyfelder, and Meckel, quoted by Fürst. Some writers accept these, some do not.

Through the courtesy of Dr. W. C. Hollopeter, I am enabled to add the following case, which occurred in his service at the Philadelphia General Hospital. The clinical notes are abstracted from those of the interne, Dr. Marek.

19. F. M., boy, aged eight years. Admitted November 7, 1915. Good proportion and development, but poorly nourished. Family and previous history negative. Sick one week prior to admission, with chills and fever. Complains of pain in left knee and muscles of legs. Left knee slightly swollen.

Chest expansion fair, but diminished on left side. Lungs: except at apex, dulness posteriorly on left side extending to midaxillary line; no dulness at apex in front or posteriorly; tubular breath sounds heard posteriorly as far as midline of left side. Right lung: no dulness; breath sounds harsher. Heart: apex displaced to midaxillary line and in fourth interspace. Right border two inches to left of sternum. Accentuated second sound. Blowing systolic murmur, heard best at apex and transmitted to left. Heart sounds heard well over area of dulness described in back. Diagnosis: Acute articular rheumatism; acute endocarditis.

November 8. Dulness in back over left lung is marked and no breath sounds audible at base. Above root of lung tubular breathing. Right lung normal except for exaggerated breath sounds. Cardiac impulse over thoracic wall in midaxillary line. Roentgen-ray examination: There is effusion of the left side of the chest. The heart cannot be defined owing to shadow of fluid.

November 9. Two attempts to aspirate fluid from pleural cavity failed.

November 12. Breath sounds audible when puncture was made, but not in midaxillary line when murmur was loud and pronounced.

November 13. Retraction of intercostal muscle in fourth interspace of left side.

November 14. Breath sounds more audible over apex of left lung.

November 19. Death.

The body came to autopsy November 20, with the following clinical diagnosis: Acute articular rheumatism; acute endocarditis; pericarditis with effusion; pleurisy with effusion.

The autopsy notes bearing on the condition here reported are briefly these:

Diaphragm is at fifth interspace on each side. Removal of sternum reveals pulmonary tissue occupying entirely the exposed area. The right pleura anteriorly and laterally has firm adhesions. The left lung is absent, the right lung extending well beyond the left costochondral line and the large pericardial sac occupying the remainder of the left side of the thorax. The pericardium contains 75 c.c. of serum. Left branch of pulmonary artery and left pulmonary veins are lacking. Two veins from right lung enter left auricle.

The right lung (Fig. 1) is large, the upper lobe being approximately twice the usual size. A projection to the left from the upper extremity forms a second apex half the width of the right, the former extending beneath the left clavicle and first rib. At the lower margin of the upper lobe is a projecting tongue, 3 by 3 cm., forming a rudimentary lobe. The middle lobe is of the usual size, but projecting partly from it and partly from the upper lobe is a lobe-like mass 3 by 4 cm. Roughly speaking the lung has a sem-

FIG. 1.—Malformed right lung, left lung absent. Postero-internal view. The lung especially the upper lobe, is large. There are two apices, the left longer and more pointed; this extended under the left clavicle and gave left apical breath sounds. Left bronchus 2 cm. long, terminating in a small mass of rudimentary lung tissue.

blance of five lobes. The lower lobe is large and has a number of small subpleural hemorrhages. The diaphragmatic surface of the lower lobe has a thin covering of fibrin. There is no evidence of consolidation. The right primary bronchus is normal. The left, which is a trifle smaller, ends 2.5 cm. below the bifurcation in a blind pouch of soft, grayish tissue, 1.2 by 0.7 cm. in size.

The heart, other than huge vegetations on the mitral leaflets, shows no noteworthy abnormality.

Anatomical Diagnosis: Acute vegetative mitral valvulitis; hydropericardium; chronic adhesive pleuritis of right side, with acute fibrinous pleuritis at base; absence of left lung; hypertrophy of right lung; cloudy swelling of heart and kidneys; fatty infiltration,cloudy swelling, and red infarct of liver; multiple embolic infarcts of kidneys and spleen; embolic gangrene of three small toes of left foot.

Sections through the terminal portion of left bronchus and the tissue over it show a bronchial wall containing cartilage surmounted by cellular connective tissue without muscle or glands. The surface

FIG. 2.—Section of tissue covering end of short left bronchus. Near center are several indistinct spaces lined by cuboidal epithelium that probably are rudimentary alveoli.

is partly covered by cuboidal or low columnar epithelium. Surmounting the bronchus is soft, cellular fibrous tissue, with occasionally an illy defined space (Fig. 2) lined by epithelium, suggestive of alveolus or bronchus, but not typical of either; rudimentary lung tissue appears the best term to apply to it.

Of these 19 cases of absence of one lung, 13 were of the left and 6 of the right, showing a predilection for left-sided pulmonary aplasia that is not satisfactorily explained on anatomical grounds. Interference with blood supply in early embryonic life is supposed to be the cause in all cases.

Anomalies other than those of the bloodvessels directly concerned were present in some of the cases, but not in others. In all of them the chest externally was symmetrical, the opposite lung, the heart, or fluid taking the place of the missing organ; in one, part of the intestines were in the thorax. This is important as increasing the difficulty of diagnosis during life and is also an argument against the case of Chilaiditi[15] being one of pulmonary aplasia. His patient is a boy, aged ten years, in whom he has diagnosticated agenesis of left lung by the roentgen rays. The left half of the thorax is flattened, however, and the left shoulder is lower than the right. Chilaiditi[15] admits that in such a case one would naturally think first of inflammatory contraction as the cause of the deformity, but says the physical signs in his patient are against this supposition. There is no difficulty in breathing, and percussion gives a clear note anteriorly two fingers beyond the middle line to the left. Posteriorly there is paravertebral clearness 2 to 3 cm. on the left side, otherwise there is absolute dulness. There is bronchial breathing over the left apex. The heart boundary is not to be determined by percussion. The apex beat is probably at the level of the nipple and 2 cm. toward the axillary line.

Meyer[16] believes he has under observation a case of aplasia of the left lung in a man, aged twenty-seven years. The subject has a well-developed thorax. The apex beat is in the midaxillary line. There is normal lung resonance anteriorly except in the left supraclavicular region (where there is slight dulness) and over the heart. Posteriorly there is complete dulness on the left side except a zone two and a half fingers broad along the vertebral column from the sixth to the twelfth rib. Meyer believes the diagnosis of aplasia of the left lung is substantiated by the roentgen-ray findings. He states that if the condition is acquired the thorax usually sinks in while in congenital cases, or real aplasia, the other lung hypertrophies and prevents sinking, hence the chest is symmetrical. Neisser has observed in the Stettin Hospital a case essentially like that of Meyer.

It may be, therefore, that the diagnosis of absence of a lung may be made clinically, although this has not yet been done and proved by autopsy. The usual enlargement of the one lung furnishes the presence of pulmonary tissue and its physical signs on the side of the absent organ; this does not suggest to the clinician the lack of an entire lung. The extreme rarity of the condition, of course, renders it unobtrusive as a possibility.

The duration of life in cases of absence of one lung is usually short, but this probably depends partly upon other circumstances. The condition is not incompatible with adult life, one of the subjects being twenty years, two each twenty-four years, and one sixty-five years of age; another is recorded as being a "young man."

BIBLIOGRAPHY.

1. Rev. mens. des mal. de l'enfance, 1884, ii, 554.
2. Abhandlungen der K. K. Josephischen Mediz-Chirurg., Akademie zu Wien, 1787, Bd. i, 271.
3. Wchnschr. f. d. ges. Heilkunde, 1837, p. 536.
4. Casper's Wchnschr., 1837, cited by Fürst, Gerhardt's Handb. d. Kinderkr., 1878, iii, Heft 2, 553.
5. Anatomy of the Human Body, cited by Schuchardt and others.
6. Allg. wien. med. Ztg., 1862, 78.
7. Oesterr. Ztschr. f. Prakt. Heilk., 1870, xvi, 7.
8. Correspond. Med., Madrid, 1874, ix, 372.
9. Virchows Archiv, 1885, cii, 11.
10. Trudi Obshtsh. dietsk Vrach., Mosk., 1894–1895, iii, 32–39.
11. Inter. Monatschr. f. Anat. u. Physiol., 1895, xii, 24.
12. Jour. Am. Med. Assn., 1901, xxxvii, 701.
13. Proc. Anat. Soc. Great Britain and Ireland, 1901–1902, p. 38.
14. Zieg. Beitr. z. path. Anat., 1905, xxxvii, 487.
15. Fortschr. a. d. Geb. d. Röntgenstrahlen, Hamburg, 1910, xv, 108–114.
16. Archiv. f. Entwicklungsmechanik, 1910, xxx, teil 1.

THE USE OF IMMUNE SERUM IN THE TREATMENT OF WHOOPING COUGH.*

By Adrien Bleyer, M.D.,

st. louis.

(From the Pediatric Department of the Medical Department of Washington University, St. Louis.)

Very satisfactory results with immune serum have been obtained in two diseases of lower animals: in epidemic jaundice the blood of guinea-pigs which have recovered from this disease will inactivate the virus, active blood being neutralized by one-hundredth part of convalescent's blood.[1,2] In hog cholera immunity is conveyed by injections of convalescent's blood,[3] which becomes life-long upon the addition of antigen such as the blood or tissues of an active case.[4]

In no disease in man have such results been obtained with immune blood. In scarlet fever, when used early in cases that have not become septic in type, results have occasionally been obtained; these are not yet consistent.[5,6,7,8,9,10,11,12,13,14,15,16,17,18] Mixed convalescent's blood has been used in measles.[19] Protective powers have been observed in mumps from small doses (6 to 8 c.c.) injected into muscle[20] in an institutional epidemic in which 33 per cent. of (134) susceptible children contracted mumps; no case occurred among those (17 children) treated. The blood of animals (cat) inoculated with saliva from cases of human parotitis is found to modify the course of such inoculations in other animals.[21] In

* Read at the second annual meeting of the Central States Pediatric Society, in St. Louis, October 18, 1916.

poliomyelitis convalescent's blood will inactivate the virus;[22] immune substances have been found both in the blood of monkeys[23 24 25 26] and human beings,[27] and therapeutic properties were seen when the administration of the serum was made within eighteen to twenty-four hours after the inoculation of the virus into the brain or nose.[28] In a recent summary of this work in poliomyelitis[29] it is said that in the case of monkeys in which the virus does not exceed a certain dose the disease can be prevented or the onset of paralysis delayed. Human serum is found effective for monkeys.[30] A series of 32 human cases in which immune serum from human cases was injected intraspinally is reported;[31 32 33] there occurred in these about the same incidence of deaths, paralysis, and recoveries as occur among cases not so treated; there is another series of 4 cases with similar results,[34] and a report of 2 cases in which serum was used from persons who had recovered years before[35] (it is said that the neutralization test remains positive after poliomyelitis for a number of years*).[36] Convalescent's blood has been used in epidemic meningitis[37] and in pneumonia[38] without great success.

Because of these data it seemed worth while to try this method of treatment in whooping cough. It is now usually thought that whooping cough is a specific infectious disease; during the course of the second or third week, antibodies appear which are specific by agglutination[39] and by complement tests.[40 41] For the purpose of determining the value of this method, injections of human blood were carried out in the early weeks of this disease in 45 cases. These were divided into three groups of 15 cases each. In Group A the blood injected was from persons who were convalescent or who had recovered from whooping cough within three months. In Group B the blood was from persons who had had the disease at more remote periods, and in Group C from persons who, so far as they knew, had never had it. Groups B and C were designed as controls to A.

The ages of the children in all groups averaged under three years: in Group A, in which convalescent's blood was used, 5 were in the first half year of life, 1 was five weeks old, and 1 thirty days old. The stage of the disease at which the treatment was given was about the same in the three groups; in Group A it was begun in the first week in 2 cases, in the second week in 5 cases, in the third weeks in 7 cases, and in the fourth week in 1 case. Dosage was gauged in a rough way to body weight of donee, from one-tenth to one-fifth of the computed volume of blood of donee was given; this varied between 40 and 125 c.c., divided into two, three, or four doses and injected into muscle (gluteus). Discoloration often followed the injections in very young infants; in a few there was

* Since this bibliography was prepared, another series of 15 cases has been reported (C. W. Wells: Jour. Am. Med. Assn., October 21, 1916, No. 17, lxvii, 1211).

induration for a day or two; there were no infections, and temperature reactions insofar as could be told in this disease did not occur. The injections in every case were completed within a week in order to avoid hemolytic reactions; reactions to new proteins were not observed. The blood used was from a single donor in ten, from two in four, and from three in one. Blood not used at once was citrated to 1 per cent. (in this amount sodium citrate is said not to affect antibody).[42] The usual examination of donors, including Wassermann reactions on the bloods of non-relatives, were made.

The results of the treatment in the three groups may be summarized: In Group A of 15 children whose average age was twenty-eight months, who received convalescent's blood during the early weeks of whooping cough, there occurred no deaths and no serious complications; the course of the disease was, however, in no definite way different than is usually seen, and was not appreciably influenced by the treatment except in 3. This is a very small proportion, and it is more than likely that in 15 cases 3 of them might very well run an unexpectedly mild course without attracting a great deal of notice. The blood pictures of 2 of these, however, was interesting: In Case 4, during the third week of the disease, a 50,000 white count came down after 60 c.c. of convalescent's blood to 18,000 and the mononuclear percentage fell from 74 to 50; this drop was coincident with clinical improvement; this was a hand-fed baby of five months who weighed but 3860 grams.

In Cases 8 and 11 a transitory hyperleukocytosis followed injections of the blood, and was succeeded in each instance by a drop to well below the original counts; changes in mononuclear percentages accompanied these drops. The shortest course of any of these cases was that of Case 11, four weeks; no shortening of the course of the disease was seen in any of the others.

In Group B, in Case 1, in which the blood used was from the mother who had had pertussis twenty years before, quite as satisfactory improvement occurred as in any case in Group A; in this group there were two pneumonias which recovered. There were also two pneumonias in Group C with one death, and in this group there was one case which seemed to have been very favorably affected by the injections of normal blood.

In explanation of these results it may be said that in some diseases injections of normal blood have brought about improvement, and that immunity may be increased at times by injections of normal blood,[43] that this has also occurred after injections of other things, such as protease,[44] lipase, ferments (trypsin), or drugs (kaolin).[45 46] Hyperleukocytosis, such as occurred in several cases in this series, has assisted immunity in other diseases (arthritis, typhoid[47 48]), so for lack of consistency in the results obtained in these cases of whooping cough it is not possible to ascribe any of them to a specific action of the blood injected.

poliomyelitis convalescent's blood will inactivate the virus;[22] immune substances have been found both in the blood of monkeys[23 24 25 26] and human beings,[27] and therapeutic properties were seen when the administration of the serum was made within eighteen to twenty-four hours after the inoculation of the virus into the brain or nose.[28] In a recent summary of this work in poliomyelitis[29] it is said that in the case of monkeys in which the virus does not exceed a certain dose the disease can be prevented or the onset of paralysis delayed. Human serum is found effective for monkeys.[30] A series of 32 human cases in which immune serum from human cases was injected intraspinally is reported;[31 32 33] there occurred in these about the same incidence of deaths, paralysis, and recoveries as occur among cases not so treated; there is another series of 4 cases with similar results,[34] and a report of 2 cases in which serum was used from persons who had recovered years before[35] (it is said that the neutralization test remains positive after poliomyelitis for a number of years*).[36] Convalescent's blood has been used in epidemic meningitis[37] and in pneumonia[38] without great success.

Because of these data it seemed worth while to try this method of treatment in whooping cough. It is now usually thought that whooping cough is a specific infectious disease; during the course of the second or third week, antibodies appear which are specific by agglutination[39] and by complement tests.[40 41] For the purpose of determining the value of this method, injections of human blood were carried out in the early weeks of this disease in 45 cases. These were divided into three groups of 15 cases each. In Group A the blood injected was from persons who were convalescent or who had recovered from whooping cough within three months. In Group B the blood was from persons who had had the disease at more remote periods, and in Group C from persons who, so far as they knew, had never had it. Groups B and C were designed as controls to A.

The ages of the children in all groups averaged under three years: in Group A, in which convalescent's blood was used, 5 were in the first half year of life, 1 was five weeks old, and 1 thirty days old. The stage of the disease at which the treatment was given was about the same in the three groups; in Group A it was begun in the first week in 2 cases, in the second week in 5 cases, in the third weeks in 7 cases, and in the fourth week in 1 case. Dosage was gauged in a rough way to body weight of donee, from one-tenth to one-fifth of the computed volume of blood of donee was given; this varied between 40 and 125 c.c., divided into two, three, or four doses and injected into muscle (gluteus). Discoloration often followed the injections in very young infants; in a few there was

* Since this bibliography was prepared, another series of 15 cases has been reported (C. W. Wells: Jour. Am. Med. Assn., October 21, 1916, No. 17, lxvii, 1211).

induration for a day or two; there were no infections, and temperature reactions insofar as could be told in this disease did not occur. The injections in every case were completed within a week in order to avoid hemolytic reactions; reactions to new proteins were not observed. The blood used was from a single donor in ten, from two in four, and from three in one. Blood not used at once was citrated to 1 per cent. (in this amount sodium citrate is said not to affect antibody).[42] The usual examination of donors, including Wassermann reactions on the bloods of non-relatives, were made.

The results of the treatment in the three groups may be summarized: In Group A of 15 children whose average age was twenty-eight months, who received convalescent's blood during the early weeks of whooping cough, there occurred no deaths and no serious complications; the course of the disease was, however, in no definite way different than is usually seen, and was not appreciably influenced by the treatment except in 3. This is a very small proportion, and it is more than likely that in 15 cases 3 of them might very well run an unexpectedly mild course without attracting a great deal of notice. The blood pictures of 2 of these, however, was interesting: In Case 4, during the third week of the disease, a 50,000 white count came down after 60 c.c. of convalescent's blood to 18,000 and the mononuclear percentage fell from 74 to 50; this drop was coincident with clinical improvement; this was a hand-fed baby of five months who weighed but 3860 grams.

In Cases 8 and 11 a transitory hyperleukocytosis followed injections of the blood, and was succeeded in each instance by a drop to well below the original counts; changes in mononuclear percentages accompanied these drops. The shortest course of any of these cases was that of Case 11, four weeks; no shortening of the course of the disease was seen in any of the others.

In Group B, in Case 1, in which the blood used was from the mother who had had pertussis twenty years before, quite as satisfactory improvement occurred as in any case in Group A; in this group there were two pneumonias which recovered. There were also two pneumonias in Group C with one death, and in this group there was one case which seemed to have been very favorably affected by the injections of normal blood.

In explanation of these results it may be said that in some diseases injections of normal blood have brought about improvement, and that immunity may be increased at times by injections of normal blood,[43] that this has also occurred after injections of other things, such as protease,[44] lipase, ferments (trypsin), or drugs (kaolin).[45] [46] Hyperleukocytosis, such as occurred in several cases in this series, has assisted immunity in other diseases (arthritis, typhoid[47] [48]), so for lack of consistency in the results obtained in these cases of whooping cough it is not possible to ascribe any of them to a specific action of the blood injected.

BIBLIOGRAPHY.

1. P. Uhlenhuth and W. Fromme: Med. klin., Berlin, November 14, 1915, No. 46, xi, 1253.
2. R. Inaba, Y. Ida, R. Hoki, R. Kaneko, and H. Ito: Jour. Exper. Med., Baltimore, March, 1916, No. 3, vol. xxiii.
3. M. Dorset, C. N. McBride, and W. B. Niles: Bull. No. 102, Bureau of Animal Industry, Department of Agriculture, U. S. A., 1908.
4. M. Dorset: Farmers' Bull. No. 379, U. S. Department of Agriculture, 1909.
5. C. W. Duval and M. J. Couret: Tr. Assn. Am. Phys., Washington, D. C., May 11, 1916.
6. R. V. Conway: University of Missouri.
7. E. Reiss and P. Jungmann: Deutsch. Arch. f. klin. Med., 1912, cv, 70.
8. C. Rowe: Med. klin., 1913, ix, 1978.
9. Koch: München. med. Wchnschr., 1913, lx, 2611.
10. Wm. S. Barker: Arch. Ped., 1914, xxxi, 599.
11. A. Zingher: Arch. Ped., 1914, xxxi, 917.
12. A. Zingher: Arch. Ped., 1915, xxxii, 291.
13. A. Zingher: Jour. Am. Med. Assn., 1915, lxv, 875.
14. A. Zingher: New York State Jour. of Med., March, 1916, No. 3, xvi, 105.
15. Wm. H. Park: Discussion Meeting., New York Academy of Medicine, February 11, 1915.
16. Matthias Nicoll: Ibidem.
17. Wm. Shannon: Ibidem.
18. Huber, Blumenthal, von Leyden, Rumpel, Scholz.
19. Am. Jour. Nursing, March, 1916.
20. A. F. Hess: Am. Jour. Dis. Child., August, 1915, No. 2, x, 99.
21. M. Wollstein: Jour. Exper. Med., Baltimore, March, 1916, No. 3, xxiii, 265.
22. Osler and McCrae: Encyclopedia of Medicine.
23. P. H. Romer and K. Joseph: München. med. Wchnschr., 1910, lvii, 568.
24. Levaditi and Landsteiner: Compt. rend. Soc. de biol., 1910, lxviii, 311.
25. Simon Flexner and P. A. Lewis: Seventh Note, Jour. Am. Med. Assn., May 28, 1910, p. 1780.
26. Levaditi and A. Netter: Presse méd., 1910, xviii, 268.
27. Simon Flexner and P. A. Lewis: Seventh note, Jour. Am. Med. Assn., May 28, 1910, footnote 2.
28. Ibidem.
29. Simon Flexner: Jour. Am. Med. Assn., August 19, 1916.
30. Simon Flexner and H. L. Amoss: Jour. Exper. Med., 1914, xx, 249.
31. A. Netter: Bull. de l'acad. de méd., 1914, lxxviii, 522.
32. A. Netter: Bull. de l'acad. de méd., October 12, 1915.
33. A. Netter: Arch. de méd. des Enfants, Paris, December, 1915, xviii, 2.
34. A. Sophian: Jour. Am. Med. Assn., August 5, 1916, p. 426.
35. A. Netter and M. Salanier: Bull. et mém. Soc. med. des hôp. de Paris, March 10, 1916.
36. Simon Flexner: Jour. Am. Med. Assn., September 24, 1910, p. 1105.
37. McKenzie and Martin: Brit. Med. Jour., October 31, 1908, p. 1341.
38. Personal communication: Dr. Kelso, Unit I, City Hospital, St. Louis.
39. O. R. Povitzky and E. Worth: Arch. Int. Med., Chicago, February, 1916, xvii, 2.
40. J. Bordet and O. Gengou: Ann. de l'Instit. Pasteur, 1906, xx, 731.
41. M. P. Olmstead and O. R. Povitzky: Jour. Med. Research, January, 1916, xxxiii, 3.
42. Wm. H. Park: Discussion Meeting, New York Academy of Medicine, February 11, 1915.
43. K. Sakagami: Lancet, London, January, 1916, No. 15, i, 127.
44. J. W. Jobling and Wm. Petersen: Jour. Exper. Med., 1915, xxii, 568.
45. Ibidem: Jour. Am. Med. Assn., 1916, lxvi, 23.
46. Arkin: Am. Jour. Physiol., Baltimore, 1916, xl, 148.
47. F. P. Gay and E. J. Claypole: Arch. Int. Med., November, 1914, p. 662.
48. Miller and Lusk: Jour. Am. Med. Assn., June 3, 1916, p. 1756.

AURICULAR FIBRILLATION: SOME CLINICAL CONSIDERATIONS.

By Samuel A. Levine, M.D.,
BOSTON.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston.)

Auricular fibrillation is a condition in which numerous irregular, very rapid impulses are sent out by the auricles. The auricles do not actually contract, but, on the contrary, remain twitching in diastole. The ventricles, however, respond to a small portion of the impulses and contract in a grossly irregular fashion both as to rate and strength. The condition has been called "delirium cordis" and "pulsus irregularis perpetuus." In the great majority of cases it is easily recognized by auscultation at the apex and palpation of the radial pulse. The absolute arrhythmia heard over the precordium, generally with a rate over 100 (when the patient is first seen), together with a pulse deficit (difference between the apex and radial counts) in a patient with cardiac failure indicate that the auricles are fibrillating. In not more than 10 per cent. of the cases, according to Lewis,[1] will the above proposition not be true and in not more than 10 per cent. will this condition be confused with other arrhythmias, especially numerous extrasystoles. Considerations that will appear later in this paper will help to diminish this error still further.

During the past several years considerable work has been done, using the newer methods of cardiac diagnosis, which has given us a clearer conception of auricular fibrillation. The great importance of this condition is indicated by its frequency, 128 different cases having been observed at the Peter Bent Brigham Hospital in thirty months; while during the same period of time there were admitted 146 cases of such a common disease as lobar pneumonia. These figures become more striking when one considers that the cases of pneumonia are not apt to return, while the cardiac cases keep coming back frequently to the wards, though in the figures given above readmissions are not included. In fact, it is not a rare occurrence to see 10 cases of auricular fibrillation at one time in the wards where there are about eighty beds. Its importance is also indicated by the fact that it is generally a permanent irregularity, and if untreated, seriously embarrasses the circulation. At the same time it can be said there is no group of cardiac cases that responds so well to proper treatment.

For the above reasons a clinical study has been made of all the cases of auricular fibrillation observed at the Peter Bent Brigham Hospital during a period of two and a half years. Only those

[1] From a lecture given at the Peter Bent Brigham Hospital, October, 1914.

cases have been considered in which the diagnosis was made by electrocardiographic tracings. The special points that were sought for in analyzing the records were a previous history of rheumatic fever or chorea, the presence of organic mitral disease, and the age of the patient. It became a matter of interest whether any data of diagnostic or prognostic value could be drawn from a large group of cases by studying the relation between the presence or absence of a past history of rheumatic fever, the signs or lack of signs of organic mitral disease, and the age of the patient. Other clinical points, such as the importance of syphilis in auricular fibrillation and the differentiation between organic and relative mitral insufficiency, also have been considered.

As will be shown below, there seemed to be a fairly intimate relationship between the previous history of rheumatic fever and the subsequent development of organic mitral endocarditis (generally mitral stenosis), with the inception of auricular fibrillation. Lea[2] several years ago, using polygraphic tracings in his study of 69 cases of auricular fibrillation, found rheumatic fever or chorea in 56.6. per cent. There was another definite group of cases in our series in which there was no history of rheumatic fever, no signs of mitral disease, and auricular fibrillation was present; these were all cases of cardiac sclerosis or chronic myocarditis. In the entire series there were 128 cases equally divided between males and females, *i. e.*, 64 males and 64 females. (See Table.) The average age of all the cases was 47.3 years (ranging from seventeen to seventy-five years). The average age of the males and females was practically the same, 48 for the former and 46.6. for the latter.

Syphilis as an Etiological Factor. The role that syphilis plays as an etiological factor in auricular fibrillation was found not to be very important. There were only 11 cases that had a positive Wassermann reaction, *i. e.*, 8.6 per cent., the test having been done as a routine on all cases. When we compare this figure with the general average of all cases admitted to the medical wards, which according to Walker and Haller[3] was 12 per cent., we see that syphilis was less common in cases of auricular fibrillation than in those not having it. The 11 cases consisted of 2 with aneurysms of the aorta, 2 of syphilitic aortitis, and 7 which either had chronic myocarditis or chronic mitral endocarditis, or both. It is noteworthy that a fair number of chronic heart cases when first seen have an enlarged liver resulting from a relative regurgitation through the tricuspid valve and become jaundiced. A positive Wassermann reaction under these circumstances may later prove to be negative if repetition is made after the jaundice has disap-

[2] Some Points in Relation to the Etiology of Auricular Fibrillation, Quart. Jour. Med., 1910–11, iv, 423.

[3] Routine Wassermann Examination of Four Thousand Hospital Patients, Jour. Am. Med. Assn., 1916, lxvi, 488.

peared. This happened in at least one of our cases. It is evident from these figures that syphilis plays an unimportant part in the etiology of auricular fibrillation.

Statistical data.	Number of cases.	Per cent.
Auricular fibrillation	128	
Persistent auricular fibrillation	110	85.9
Transient auricular fibrillation	18	14.1
Males	64	50.0
Females	64	50.0
Average age of males (limits seventeen to seventy-five years)	48.0	
Average age of females (limits twenty to seventy-two years)	46.6	
Wassermann positive in the blood	11	8.6
Persistent Auricular Fibrillation:		
Group I. Rheumatic history and mitral endocarditis	39	35.5
Males	15	
Females	24	
Average age of males	35.0	
Average age of females	38.4	
II. No rheumatic history and no mitral endocarditis	34	30.9
Males	23	
Females	11	
Average age of males	57.5	
Average age of females	58.9	
III. Unclassified	37	33.6
Total number of cases in Groups I and III with definite rheumatic history	48	43.6
Autopsy Examinations:		
Hearts examined	261	
Over fifty years of age	107	
Showing chronic mitral endocarditis	2	
Under fifty years of age	154	
Showing chronic mitral endocarditis	21	

Transient Auricular Fibrillation. Although auricular fibrillation was at first considered a permanent irregularity, and was called "pulsus irregularis perpetuus," it is now quite definitely known that it need not be so. In fact, K. Fahrenkamp,[4] in a review of 120 cases of auricular fibrillation, all diagnosed by electrocardiograms, found 4 transient cases *i. e.*, 3.5 per cent. It is necessary at this point to decide what is to be called transient and what permanent auricular fibrillation. There are some cases which have definite repeated attacks of palpitation and tachycardia just like the ordinary paroxysmal auricular tachycardia, except that the heart's action is absolutely irregular. Short periods of fibrillation are often observed in cases of auricular flutter after digitalis has been given and before the normal rhythm is resumed. Transient auricular fibrillation also occurs under very varied conditions, *i. e.*, during acute rheumatic fever, postoperative, in hyperthyroidism, etc. In addition it is observed rarely as a terminal event lasting from a few hours to a few days. All cases of this series that have not been observed to become regular in rhythm have

[4] Vorübergehende komplette Herzunregelmassigkeiten unter dem klinischen Bilde der Arhythmia perpetua mit Boebachtungen über Vaguswiskung. Deutsch. Arch. f. klin. Med., 1914, cxvii, 1.

been considered as cases of permanent auricular fibrillation, and those that were definitely proved to have returned to a normal rhythm were grouped as transient. Of the 128 cases, 110 were persistent and 18 were transient (14.1 per cent.). This is a much higher figure than has heretofore been noted.

One has to exercise the greatest care in making the diagnosis of transient fibrillation. If one depended on polygraphic tracings or merely on auscultation frequent errors would be made, as has been shown by Fahrenkamp.[5] Numerous extrasystoles together with a sinus arrhythmia might cause a very irregular pulse, and this would change into a normal rhythm, with rest in bed and simple sedatives, as the extrasystoles disappeared. This, of course, wrongly would have been considered a case of transient fibrillation. Then, again, if an absolutely irregular heart action becomes perfectly regular, as determined by auscultation or palpation of the radial pulse, it is no proof that the auricles have stopped fibrillating. Two cases of this series acted in such a way, and at first were thought to be transient cases. This was supposed to have been brought about by digitalis. Careful examination of the electrocardiograms showed that the auricles were still fibrillating, but that there was complete auriculoventricular heart-block with a regular ventricular rhythm. In both of these cases the ventricular rate was rapid, which did not make one immediately think of an idioventricular rhythm. The possibility of a rapid regular ventricular rate in auricular fibrillation is mentioned by Lewis.[6] The ventricular rate of the first case was 62 and that of the other was 110. Furthermore, the frequency with which transient fibrillation will be noted will in a great measure depend on how carefully the heart rhythm is observed and how frequently electrocardiograms are taken. This might explain the comparatively high incidence of transient cases found in this series.

Of the 18 cases of transient auricular fibrillation here observed, 1 occurred during the lysis of pneumonia, similar to one of the cases described by Krumbhaar,[7] 1 in hyperthyroidism, 1 postoperative (avulsion of the sensory root of the trigeminus for trigeminal neuralgia),[8] 2 during acute rheumatic fever, 4 following auricular flutter, 4 as a result of active digitalis therapy, and 6 were spontaneous or idiopathic cases. Among these latter there were 3 who had chronic myocarditis (2 with and 1 without chronic nephritis similar in type to the cases described by Robinson);[9] 1 had cancer of the esophagus, 1 chronic alcoholism, and 1 chronic

[5] Loc. cit.

[6] Clinical Electrocardiography, London, 1913, p. 95.

[7] Transient Auricular Fibrillation, an Electrocardiographic Study, Arch. Int. Med., 1916, xviii, 263.

[8] This last case is counted twice because the fibrillation followed a short period of auricular flutter.

[9] Paroxysmal Auricular Fibrillation, Arch. Int. Med., 1914, xiii, 298.

endocarditis of the aortic and mitral valves. Cohn[10] has observed transient fibrillation during pneumonia in a large portion of his cases, 12 out of 123, 7 of whom had had no digitalis. Two interesting cases have been observed during the past year who were not patients in the hospital and have therefore not been included in this study. They complained of frequent attacks of palpitation, otherwise they were well. Nothing abnormal could be found on careful examination except the arrhythmia, which was a transient auricular fibrillation. Both happened to be well developed athletic young men. Gossage and Hicks[11] refer to the possibility that patients previously well may suddenly develop auricular fibrillation. It therefore can be stated that the transient form of auricular fibrillation may exist in otherwise normal individuals as well as under many various abnormal conditions.

On careful questioning one is impressed by the frequency with which patients suffering from auricular fibrillation have complained of previous attacks of palpitation. Quite often the symptoms of shortness of breath, pain in the chest, cough, etc., have had a sudden onset, and they were not always precipitated by exertion. In fact, some of the patients complained that the trouble was first noticed when they suddenly awoke during the night and found the heart palpitating. In some cases the history of attacks of palpitation was repeated, with periods free from symptoms in between, and extending over one or more years before the permanent state was assumed. In others there was no repetition of the attacks, and on the contrary the symptoms of circulatory failure seemed to date definitely from the onset of auricular fibrillation. It would seem that many of the cases of permanent fibrillation have gone through transient attacks and that the symptoms complained of by the patient are intimately connected with the occurrence of the irregularity.

Persistent Auricular Fibrillation. There were 110 cases of persistent fibrillation which arbitrarily have been divided into three groups. The first includes all cases who had a definite history of rheumatic fever or chorea and had signs of chronic organic mitral disease. The second includes all those who gave no history of rheumatic fever or chorea and who were diagnosed[12] as having no organic mitral disease. The third group includes all of the remaining cases. One is immediately impressed by the natural obstacles to such a classification. The histories are taken by different house officers. Occasionally one forgets either to ask or at least to record definitely whether the patient had or had not

[10] Irregularities in Pneumonia. Unpublished.

[11] On Auricular Fibrillation, Quart. Jour. Med., 1912–13, vi, 435.

[12] In all these considerations the diagnosis taken was the one which was finally made by Dr. H. A. Christian, physician-in-chief, who saw the larger part of the patients, examined the records, and approved of the diagnoses of all the cases.

had acute rheumatic fever or chorea, although it must be said that in all but a few cases there was some statement on this point. Furthermore, some patients knew very little English and probably answered to questions they hardly understood. Finally, one might obtain a history of rheumatic pains or rheumatism. This was generally followed by a short description of the condition which identified it; but unfortunately this description was lacking in some instances and was unsatisfactory in others, so it was decided, in this study, to include in the first two groups only those cases in which a definite statement was made and which had the two qualifications required as mentioned above. If a case had a definite history of rheumatic fever and had no evidence of mitral disease it fell in the third or exceptional group; if the past history was vague, or the clinical diagnosis doubtful, it was included in this last group.

It was found by this method that 39 cases (15 males and 24 females), or 35.5. per cent., of the cases of permanent fibrillation, fell in the first group, *i. e.*, having a definite history of one or more attacks of rheumatic fever or chorea and showing signs of chronic mitral endocarditis. Most of these showed definite evidence of mitral stenosis, generally with mitral insufficiency. Two cases were included here with some hesitation, because although there was definite evidence of organic aortic disease the signs overshadowed those of mitral disease. They both had loud murmurs of aortic stenosis and aortic insufficiency which were best heard at the base but were also present at the apex of the heart. The question as to whether there was organic mitral endocarditis was in doubt. The Wassermann blood tests were negative; one of the patients had had four attacks of rheumatic fever and the other one attack. In this respect they stand out as the only rheumatic patients who had auricular fibrillation in whom the question as to whether the mitral valve was involved was uncertain, when there were definite signs of valvular disease. These 2 cases were included in Group I, with the positive cases of mitral disease because the endocarditis was undoubtedly rheumatic in nature. The average age of the females in this group was 38.4, that of the males 35; the former were decidedly more numerous. There were only 2 cases over fifty years of age. One was a man, aged fifty-five years, who had three attacks of rheumatic fever at the ages of sixteen, forty-three, and fifty-two. He had been doing very hard physical work all his life up to the age of fifty-two years. It might well be that the first attack of rheumatic fever did not affect his heart, which would account for the late occurrence of the auricular fibrillation and the mitral disease. The other was a woman, aged fifty-six years, who belonged to a higher class in society than the average hospital patient. She had had rheumatic fever at the ages of four and thirty and chorea at twelve years. During which

infection her heart became involved it was impossible to tell. In this connection it is of interest to note that Kemp,[13] following his cases over a considerable period of time, found that 23 per cent. of them went through one or more attacks of acute articular rheumatism without clinical affection of the heart. Therefore it can be said that about one-third of the patients with permanent auricular fibrillation had both a rheumatic history and organic mitral disease, and all but 2 of this group were comparatively young.

Thirty-four, or 31.2 per cent. of the cases, were placed in the second group, *i. e.*, having no history of rheumatic fever or chorea and having no signs of chronic organic mitral disease. They were practically all cases of chronic myocarditis with or without chronic nephritis and hypertension. They frequently showed signs of peripheral arteriosclerosis. Of these there were 23 males and 11 females. The proportion of males to females is just opposite in the two groups, there being a marked preponderance of females in the first and of males in the second group. The average age of the males of the latter group is 57.5 and that of the females 58.9. This is about twenty years more than the average age of the first group. The youngest was forty-four years and the oldest seventy-five. The number of cases that could thus be put into one or the other of these two groups was 73, or 66.4 per cent. of all patients with persistent auricular fibrillation. It seems quite striking that with such narrowly limited criteria as a basis of division so large a percentage of cases could be definitely grouped. It is observed that special emphasis has been put on the fact that the valve lesion must be *chronic* and *organic*. The reason for this is that not infrequently one finds fresh minute vegetations on the mitral or aortic valves, which otherwise appear normal, and which indicate a terminal endocarditis. This, of course, could not have any important influence in the causation of the auricular fibrillation. Again, a very important consideration is the difference between organic and relative mitral insufficiency. A loud, blowing systolic murmur is frequently heard at the apex, which is transmitted to the axilla and often well heard all over the precordium. This is a common finding in senile hearts or cases of chronic myocarditis, especially if there is an associated hypertension. It signifies a functional insufficiency of the mitral valve due to a temporary or permanent dilatation of the mitral ring, but it is often confused with an organic mitral regurgitation. There does not seem to be any very definite method of differentiating the one from the other, and so one has to weigh whatever evidence there is at hand. It is for this reason that the above considerations and the autopsy findings discussed below are of some importance. If a patient is sixty years old and has no history of rheumatic fever, it is very unlikely that he has

[13] On the Prognosis of Acute Articular Rheumatism, with Special Reference to the Cardiac Manifestations, Quart. Jour. Med., 1913–14, vii, 251.

any organic mitral disease, even if there may be heard a very loud systolic murmur all over the precordium. On the other hand if the patient is thirty years old and has a definite past history of rheumatic fever or chorea and auricular fibrillation is present a systolic murmur at the apex would indicate that there was an organic mitral endocarditis. In fact, a few of the senile cases of this series were considered by some observers to have organic mitral regurgitation because of loud systolic murmurs, and showed normal valves in postmortem examination. The distinction between relative and organic mitral insufficiency is not of much importance in senile hearts, but is of considerable prognostic significance in the cases of the first group. In this group we found only two patients who were over fifty years of age, and practically all were suffering from cardiac insufficiency. Only 6 of the 39 failed to develop signs of mitral stenosis. A diagnosis of organic mitral regurgitation in a middle-aged or young person signifies that mitral stenosis may very likely develop and that the prognosis as to length of life is generally discouraging.

The third group is the most interesting because it contains the doubtful cases, and it is here that some of the above considerations can be of help in the diagnosis. Several of them readily fall into one or the other of the first two groups if studied carefully and when some questionable points are definitely determined. There were 37 cases that did not correspond to either of the first two groups. No satisfactory history was recorded, or there was a diagnosis of organic mitral disease in the absence of a history of rheumatic fever, or there was no organic mitral disease in the presence of a definite history of rheumatic fever. A careful study of these cases trying to apply the two general principles is very enlightening, *i. e.*, that a young patient who has auricular fibrillation and a definite rheumatic history very likely has chronic organic mitral disease; and secondly, that an elderly patient who has auricular fibrillation without a past history of rheumatic fever very probably has no organic mitral disease (although frequently there is a relative functional mitral insufficiency). One might further add that if a patient over fifty years old had definite signs of mitral stenosis and auricular fibrillation, very likely there was a previous history of rheumatic fever or chorea, and that this infection involved the heart late in life.

Of the 37 unclassified cases, in 6 no mention was made as to whether the patient did or did not have rheumatic fever. No further statement need be made concerning them except that there were none over fifty years of age with organic mitral disease. There were 9 who had a definite history of rheumatic fever or chorea, and yet were diagnosed as having chronic myocarditis without organic mitral disease; some of these were definitely diagnosed relative mitral insufficiency. A consideration of the

ages of these patients is very significant. One would expect that if these patients did not develop organic mitral endocarditis as a complication of the rheumatic fever (reference has been made above to the observation of Kemp[14] that 23 per cent. of rheumatics do not develop heart disease) they would belong to the group of senile hearts and average over fifty years of age. This was true of all cases except one. This was a woman, aged thirty-two years, who had chorea at the age of ten and rheumatic fever at twenty-four years. She had been complaining of dyspnea on exertion and occasional swelling of the legs, which conditions were gradually becoming worse. On physical examination a blowing systolic and a distinct diastolic murmur were heard by three observers on three different occasions. At no time was it noted that the murmurs were absent. The first heart sound at the apex and the second sound at the pulmonic area were not accentuated. Here it seems that there was sufficient evidence for a diagnosis of organic mitral endocarditis which would bring the case into Group I. Two other cases of this series were of particular interest because the house physician recorded a past history of acute rheumatic fever in them. They were both seen by the author, and one was particularly questioned on this point. His history was that of frequent attacks of acute pain in his big toes, with tenderness, redness, occasionally fever, and sometimes with involvement of the fingers. He was a typical case of gout having a very high uric acid content in his blood. The history of "acute rheumatic fever" was more likely that of acute gout. An autopsy was subsequently performed on this case and the mitral valve was found to be essentially normal. The heart was considerably hypertrophied and showed chronic cardiosclerosis. The other case with a rheumatic history was also one of gout having arteriosclerosis and chronic myocarditis without organic mitral disease. Here again the past history of frequent attacks of acute rheumatic fever might well have been that of acute gout. These 2 cases quite certainly belong to Group II. The remaining 6 of the 9 patients, who had auricular fibrillation, chronic myocarditis without organic mitral disease, and a definite history of rheumatic fever, exemplify the type in whom rheumatic fever did not injure the mitral valve, and its effect on the myocardium is questionable. If it is assumed that these 6 patients completely recovered from the rheumatic fever without injury to the heart, as is very probable, they can be considered as cases of auricular fibrillation coming as a result of chronic myocarditis with arteriosclerosis.

Five patients of this unclassified group had vague past histories; several had mild rheumatic pains or rheumatism, one had growing pains, and one did not know which diseases he had had.

[14] Loc. cit.

Although nothing definite can be said about them, it happens that the only one over fifty years of age had chronic myocarditis without any valve lesions, while the other four had organic valvular disease. Here again the difference in age incidence in the two types of auricular fibrillation is well shown, the younger ones having valvular disease and the older myocarditis.

There still remained 17 of the exceptional cases which have all been diagnosed chronic mitral endocarditis. These definitely had neither rheumatic fever nor chorea. Three had frequent attacks of acute tonsillitis. In the remaining 14 there was no previous history of any of the acute infections which are regarded as the common causes of endocarditis. No importance was attached to a history of mild sore throats which a large majority of all hospital patients evidently have had. A study of these 17 cases brought out some points worthy of mention. There were 6 over fifty years of age among them. Two were definite cases of mitral stenosis. A third which was diagnosed mitral stenosis returned eighteen months later and showed no evidence of mitral disease. A fourth, which was discharged as mitral insufficiency and questionable mitral stenosis, was examined one year later and only a blowing systolic murmur was heard. A fifth was a woman, aged sixty-seven years, who was thought to have chronic myocarditis, chronic nephritis, hypertension, and mitral stenosis, although at no time did she show a diastolic murmur or thrill. The first sound was sharp and suggested mitral stenosis. Her local physician, who had seen her at home, wrote that he had not found evidence of mitral stenosis. There certainly is some question as to whether she had endocarditis. The sixth was considered a case of chronic myocarditis with mitral insufficiency. No definite statement was made as to whether the insufficiency was relative or organic in nature. As was stated above, there generally is no way of deciding this latter point on physical signs, but as a result of the study of 261 autopsies, which will be discussed below, the age and absence of any rheumatic history point strongly against organic valvular disease. Of the 11 remaining cases who had no history of rheumatic fever under fifty years of age, 10 had definite evidence of mitral stenosis with or without accompanying aortic disease, and they all had mitral insufficiency. It can therefore be said that of all the cases of permanent auricular fibrillation there were only 4 over the age of fifty years who had definite organic mitral disease.

TREATMENT. It is well understood by all clinicians that in the treatment of heart disease one should not interest himself in treating an irregularity. The most important aim is to help the heart muscle. In this connection auricular fibrillation plays a very important role, for the irregularity results essentially in a rapid ventricular rate if the condition is left untreated. This rapid rate tires out the heart, and although the patient at first may have no

complaints and show no symptoms of circulatory failure the heart muscle is using up its reserve during this time. The cases which show the transient form of fibrillation do not generally need any treatment, except as is indicated by other manifestations, and in pneumonia when the picture becomes most alarming. Those who have persistent auricular fibrillation should be given digitalis to reduce the rapid heart action. There is no better drug for this purpose than digitalis, or strophanthin when more immediate action is desired.

The various means of treating heart failure were employed in these cases. All patients were put to bed, using back-rests and pillows to aid breathing if necessary. If edema was present they were given Karrel diet, consisting of 800 c.c. of milk a day, with no additional water until the edema was gone or was appreciably reduced. Mechanical removal of fluids from the body cavities was seldom necessary. One measure that is probably not sufficiently used in severe forms of heart failure is bleeding. It was customary with these patients to bleed all who showed evidence of extreme failure of the right side of the heart, *i. e.*, marked cyanosis, pulmonary congestion, enlarged tender pulsating liver, edema, ascites, and dilatation of the right side of the heart. Frequently, with most gratifying results, 400 c.c. to 800 c.c. were removed from the median basilic vein, the relief being immediate. This would help considerably in the course of the treatment before the other measures could begin to show their effect. Although most patients were immediately given digitalis in some form, those who were not quite so urgent were sometimes allowed to go without medication for the first twelve or twenty-four hours to observe the change brought about by rest in bed. There was no fixed dose of digitalis used, but in general the patients received one gram of the powdered leaves during the first two or three days, depending on the severity of the condition. Digitalis was continued in 0.1 gram doses three times a day until a therapeutic or toxic effect was produced. In the most urgent cases strophanthin (0.0003 to 0.0005 gram doses) was given intravenously, but always only when it was certain that no digitalis had been previously given. Another helpful drug in many of the cases was theocin. Its beneficial effects as a diuretic have recently been reviewed by Christian.[15] He showed that the best results were obtained by theocin in the cardiac cases with edema who had a good kidney function, and that if given after a course of digitalis it was especially efficient as a diuretic. In all cases particular attention was paid to procuring comfortable rest during the night.

It might hardly seem necessary to emphasize the importance of following the apex-rate in conjunction with the rate of the radial

[15] Some Studies of a Diuretic (Theocin), Arch. Int. Med., 1916, xviii, 606.

pulse in cases of auricular fibrillation. But this practice is by no means general. These two counts frequently show a marked discrepancy at first, and as the condition of the patient improves the two rates tend to coincide. In fact, it frequently happened that as the patient was improving and the apex-rate was falling the radial rate was increasing, *i. e.*, there were more beats strong enough to reach the wrist with fewer impulses arising in the ventricles. A slow radial pulse is of no significance, for it may indicate either that only a portion of the many beats are strong enough to reach the radial artery or that the heart-rate is actually slow. A slow apex-rate is always significant. In most of the cases reviewed here the heart-rate responded quite readily to the above treatment, and hand in hand there resulted an improvement in the clinical condition. There were several in whom the heart-rate was slowed without an accompanying improvement in the symptoms, and in a few neither the rate nor the clinical picture were affected.

Postmortem Observations. All the autopsy reports of the Peter Bent Brigham Hospital for about the first three years were analyzed with special reference to the age of the patient and the condition of the heart, particularly of the mitral valve. Two hundred and sixty-one subjects in whom postmortem examinations of the heart were made (some examinations were restricted to the head or abdomen) were included in this study. Of these there were 107 over the age of fifty, or 41 per cent., and only 2 had definite chronic mitral endocarditis. One was a man of sixty years who had rheumatic fever at the ages of sixteen and fifty-five years, and at autopsy the mitral valve showed slight thickening, a ragged border of the valve flaps, and some contraction of the chordæ tendineæ. The other was a man of sixty-seven years who had rheumatic fever at the ages of forty-two and sixty years. A definite fish-mouth mitral valve was found at autopsy, although the main trouble was alcoholic cirrhosis of the liver with marked ascites. It must be stated at this point that the mitral valve is not infrequently found slightly thickened in old people with arteriosclerosis, and this is generally most prominent in the aortic cusp of the mitral valve. This to the pathologist is an indication of a degenerative and sclerotic process and not of a real inflammatory chronic endocarditis. A further postmortem finding that is met with occasionally, is small fresh vegetations on the valves which are otherwise normal. They are regarded as terminal endocarditis and seem to occur under various conditions. They do not represent any evidence of a chronic endocarditis.[16] There were 154 cases under the age of fifty years of whom 21 had definite

[16] These two considerations are generally accepted according to Dr. E. W. Goodpasture, resident pathologist at the Peter Bent Brigham Hospital.

chronic organic mitral endocarditis. This is 8 per cent. of all the autopsies analyzed and 13.6 per cent. of those under the age of fifty. In striking contrast is the fact that only 1.9 per cent. of the patients dying at an older age showed organic mitral endocarditis pathologically.

CONCLUSIONS. From a study of 128 consecutive cases of auricular fibrillation diagnosed by electrocardiograms, and of 261 consecutive autopsies the following general conclusions may be drawn.

1. Auricular fibrillation is a very common condition in a general hospital being met with almost as frequently as lobar pneumonia.

2. Syphilis plays an unimportant role in the etiology of auricular fibrillation.

3. The transient form of auricular fibrillation is much more common than is ordinarily believed. Careful observations and electrocardiographic tracings are necessary in order to avoid missing the transient cases.

4. About one-third of the cases of persistent auricular fibrillation have had one or more attacks of rheumtic fever or chorea and show clinical signs of chronic organic mitral endocarditis. The average age of these patients is about thirty-seven years. About one-third of the cases have not had rheumatic fever or chorea and show no signs of chronic organic mitral endocarditis. The average age of these patients is about fifty-eight years. About one-third of the cases fall into neither Group I or II.

5. Chronic organic mitral endocarditis is quite infrequently found in patients over fifty years of age either in the living as a result of physical examination or in the dead by postmortem examination.

6. Most patients with organic mitral disease develop mitral stenosis and only a small number reach the age of fifty years.

7. The application of these principles in the properly selected cases will aid in the diagnosis of cardiac conditions, giving particular help in the differentiation of relative and organic mitral insufficiency.

TYPHOID MENINGITIS: WITH REPORT OF A CASE.

BY STANHOPE BAYNE-JONES, M.D.,
BALTIMORE, MARYLAND.

(From the Medical Clinic of the Johns Hopkins Hospital.)

THE cerebrospinal and meningeal manifestations of human infection with typhoid bacillus have an abruptness of onset, a distinctiveness of symptoms, and a prognostic value which demand

unusual attention. They may also possess an importance independent of an association with the disease typhoid fever, sufficient to render unsuitable the customary designation of "complications" or "meningeal accidents." Several cases (Nos. 6, 12, 14, 16, Table II) have been reported under the caption of "primary typhoid meningitis." In all of these, except No. 14, careful necropsies serve as the basis for the statement that the meningitis was the only evidence of typhoid infection. Lavensen believes that in the instance reported by him the nasal passage was the portal of entry. While these studies are not sufficiently conclusive to set aside the older conception that the gastro-intestinal tract is the only way by which the typhoid bacillus gains entrance to the human body, nevertheless they remove the categorical element from this dictum by indicating other possible routes of infection.

Since the study of all reported cases of meningeal disease in typhoid fever, published by Cole in 1904, it has been generally accepted that the meningeal symptoms of typhoid infection may be classified in three distinct groups. These are called:

I. *Meningism.* When there are symptoms of meningitis with no demonstrable meningeal lesions and no abnormality of the spinal fluid.

II. *Serous Meningitis.* When the symptoms of meningitis are associated with non-suppurative lesions of the meninges and a spinal fluid, showing increased tension and containing B. typhosus.

III. *Purulent Meningitis.* When the meningitis is suppurative. Here the purulent spinal fluid contains typhoid bacilli.

MENINGISM. The occurrence of meningism, or symptoms of mild, transient meningeal irritation in cases of typhoid fever, is probably so common that this syndrome no longer moves the observer to record it in the medical journals. Annual reports of this condition in the literature of typhoid fever since 1904 do not equal in number the examples of so-called "meningism" seen in this hospital during the usual summer's experience with typhoid patients.

The absence of published records of this feature of typhoid fever does not, however, signify that the symptoms are not to be regarded seriously, as possibly representing an early stage of a more dangerous process. Netter has found the mortality three times as great in cases of typhoid fever showing Kernig's sign as in those which do not exhibit it. It is obvious, therefore, that on the appearance of the signs of meningitis, efforts should be made to determine the degree of the disease of the central nervous system, and means should be directed toward the relief of these symptoms. Lumbar puncture, thus indicated, is the only means of obtaining certain information as to the meningeal condition, and at the same time, as

shown by some cases, greatly improves the condition of the patient by removing spinal fluid.

SEROUS MENINGITIS. Since 1904, instances of serous meningitis have been reported by a number of authors as follows:

TABLE I.—SUMMARY OF CASE REPORTS OF SEROUS MENINGITIS IN TYPHOID FEVER.

Case.	Year.	Author.	Spinal fluid.		
			Culture.	Pressure.	Cytology.
1	1904	Achard and Paisseau	Negative	Increased	Lymphocytosis.
2	1905	Schutze	Positive	Increased	
3	1905	Schutze	Positive	Increased	
4	1908	Silberberg	Positive	Increased	
5	1908	Nieter	Positive	Increased	
6	1909	Claret and Lyon-Caen	Positive	Increased	Polys., 60 per cent. Monos. 25 per cent.
7	1910	Stein	None	Increased	Great relief after lumbar puncture in all cases.
8	1910	Stein	Negative	Increased	
9	1910	Stein	Negative	Increased	
10	1910	Schwartz	Positive	Increased	Pleocytosis with mononuclears.
11	1910	Saquépée	Positive	Increased	Monos. 95 per cent.
12	1911	Stuhmer	Positive	Increased	Typhoid bacilli seen in smears. Globulin negative.
13	1912	Lesieur and Marchand	Positive	Increased	No leukocytic reaction.
14	1914	Hannes	Positive	Averaged 130 mm. water.	Cells were usually 11 per cu. mm. Globulin tests were negative.
15	1914	Hannes	Positive		
16	1914	Hannes	Positive		
17	1914	Hannes	Positive		

The few instances of typhoid serous meningitis seen in this clinic in the past ten years correspond to the typical cases summarized in Table I. It is seen from these observations that the spinal fluid in serous meningitis is slightly turbid, due to the mononuclear pleocytosis, and that it contains typhoid bacilli in considerable numbers. The cerebrospinal fluid in this state contains also agglutinins for Bacillus typhosus, active in dilutions as high as 1 to 100. Silberberg is of the opinion that antibacterial substances may explain the failure of organism to grow in cultures from fluids in which the bacilli are microscopically demonstrable. Serous meningitis may subside, especially after the withdrawal of the excess of spinal fluid by lumbar puncture, or it may be the early phase of a purulent meningitis. It clearly demonstrates the localization of the typhoid bacillus in the meninges. The pyogenic potentiality of the Eberth bacillus in this location is of unfavorable prognostic significance. Claret and Lyon-Caen have shown that of 13 cases of serous meningitis with typhoid bacillosis of the spinal fluid, 8 recovered while 5 died, giving a mortality of 40 per cent. of cases of typhoid fever complicated by this condition.

TABLE II.—SUMMARY OF CASES OF PURULENT TYPHOID MENINGITIS.

Case.	Year.	Author.	Sex.	Age.	History.	Autopsy.	Bacteriology.	Remarks.
1	1902	Crouchet and Buard	M	13	On 35th day of typhoid sudden onset of meningitis; purulent fluid on lumbar puncture; death 2 days later	None	B. typhosus from spinal fluid; all cultural and serological reactions typical	Not cited by Cole.
2	1905	Raymond and Siccard	M	48	During convalescence from typhoid, onset of pains in back and legs; localized purulent meningitis of lumbar cord; cured by operation	.....	Pure culture of B. typhosus from pus around spinal cord	Probably primary infection in lumbar vertebra.
3	1905	McCrae, J.	M	..	Death on 14th day of disease, after stupor, rigidity and convulsions	Acute encephalitis	Blood culture positive for B. typhosus	Data deficient.
4	1905	Stäubli, C.	M	22	Four weeks after beginning of typhoid, sudden onset of meningitis; purulent spinal fluid; death 20 days after meningeal symptoms began	Typical lesions of typhoid fever, with purulent cerebrospinal meningitis	B. typhosus from purulent spinal fluid	
5	1905	Delille, A.	F	9	Signs of meningitis on 21st day of typhoid fever; turbid spinal fluid with lymphocytosis at first; death 7 days later	Usual lesions of typhoid fever; thin yellow purulent exudate on meninges	B. typhosus from spinal fluid before death and at autopsy	Definite stage of serous meningitis at onset.
6	1908	Lavensen	F	26	Onset of meningitis on 10th day of typical typhoid fever	Purulent cerebrospinal meningitis; no other lesions	B. typhosus, with all typical reactions from spinal fluid before and after death	No intestinal lesions; no blood culture made; white blood cells, 20,640.
7	1908	Gurd and Nelles	M	25	Skull fractured 1 month before onset of typhoid fever; during typhoid, signs of meningitis and intracranial abscess at site of fracture	Operation: suppurative meningitis with abscess at site of fracture of skull	B. typhosus from localized cerebrospinal meningitis	B. typhosus from blood culture.
8	1908	Henry and Rosenberger	M	34	Seen on 6th day of disease after onset of meningitis; death 3 days later	Purulent meningitis; early lesions of typhoid in intestine	B. typhosus from spinal fluid by lumbar puncture	Blood contained B. typhosus.

9	1908	Southard and Richards	M	32	Patient was a paretic who had been in the asylum for 1 year; he died in coma after an acute illness of 1 week	Lesions of taboparesis; acute cerebrospinal meningitis, with polymorphonuclear exudate; no intestinal lesions of typhoid	B. typhosus from spinal fluid, brain and mesenteric lymph node	Aside from mesenteric lymphadenitis, no lesions of typhoid infection outside of the nervous system.
10	1909	Symmers and Wilson Milligan	M	37	Illness of 10 days with symptoms of serous meningitis; death on 15th day	None	B. typhosus from purulent spinal fluid after death	Widal reaction positive on 13th day.
11	1912	Lemierre and Joltrain	M	47	Meningitic syndrome on 3d day of typhoid fever; death on 5th day	Purulent cerebrospinal meningitis; typhoid ulcers in ileum	B. typhosus from meninges	Blood culture gave B. typhosus; white blood cells, 10,000.
12	1912	Lesieur and Marchand	M	41	Meningitis on 28th day of typhoid; death next day	Purulent meningitis; no intestinal lesions	B. typhosus from spinal fluid	B. typhosus from blood culture.
13	1912	O'Carroll and Purser	M	9	Convulsions on 5th day of typhoid fever and death 1 day later	Yellow pus in meninges; congestion and swelling of Peyer's patches	B. typhosus from spinal fluid before and after death	Widal positive.
14	1914	Planche and Lombard	M	2	Meningitis after 24 days of enteritis and pneumonia; death 3 days later	"Intestines absolutely normal;" purulent meningitis; pneumonia	B. typhosus from purlent spinal fluid	Pneumococcus from lung; leukocytes showed 85 per cent. mononuclears.
15	1914	Planche and Lombard	M	8	Meningitis on 35th day of typhoid; death in coma next day	Typhoid lesions in intestines; suppurative meningitis	B. typhosus from spinal fluid	
16	1915	Robinson	M	55	Outspoken meningitis on 2d day: death on 4th	None	B. typhosus on repeated cultures of purulent spinal fluid	Reported as "primary typhoid meningitis."
17	1915	Ortoconi and Amenille	M	28	Soldier in French Army; stuporous until 3d day, when onset of meningitis; death next day	Purulent meningitis; ulcers in ileum	B. typhosus from spinal fluid	Borderline case between serous and purulent meningitis.
18	1915	Author's case						

As an addition to Table II might be added a case reported by Arzt and Boese, in 1908, in which it was demonstrated that B. paratyphosus was the cause of purulent meningitis in a child seven weeks old.

PURULENT MENINGITIS. A review of the literature shows that purulent meningitis due to the typhoid bacillus is both an uncommon form of meningeal disease and also a rare phase of typhoid infection. Bramwell states that the meningococcus causes 50 per cent. and the pneumococcus 42 per cent. of cases of acute primary meningitis. In addition, leptomeningitis may be caused by many organisms, as a secondary process to a focus of infection elsewhere in the body. Though no definite statistics are available, it is readily seen that after the elimination of cases of meningitis due to the tubercle bacillus, the pneumococcus, and the pyogenic cocci there remain only a few to be accounted for by the organisms of influenza, diphtheria, gonorrhea, and typhoid fever. Out of 2768 cases of typhoid fever seen in this hospital between the years 1890 and 1916, there have been 5 cases of purulent meningitis due to B. typhosus. During the same period, among the adult patients of the medical clinic, there have been 290 cases of all forms of meningitis, of which 5 were caused by the typhoid bacillus. These figures give an incidence of 0.2 per cent. for meningitis in typhoid fever and 1.75 per cent. for typhoid meningitis among the bacterial meningeal diseases. Since 1904, when Cole published a collection of 15 cases, reports of 17 additional instances of purulent typhoid meningitis have appeared. These together with the case described in this paper are summarized in Table II. In all cases included in this compilation, except Nos. 2 and 3, the identification of the typhoid bacillus in the spinal fluid has been placed beyond question by detailed cultural and serological studies.

The data furnished by these cases indicate that purulent meningitis may occur at any time during the course of typhoid infection. Aside from the cases regarded as "primary typhoid meningitis," instances are presented of the occurrence of meningitis on any day of the disease from the second to the thirty-fifth. A striking fact is the invariably fatal outcome of all cases of generalized typhoid meningitis, and that usually within three days of the onset of the meningeal symptoms. The spinal fluid in a typical case is turbid, with a yellowish tinge. Typhoid bacilli are usually demonstrable in smear preparations of the fluid, and must be found by cultures before the diagnosis can be established. While the cells of the fluid are accumulations of polymorphonuclear leukocytes, the white corpuscles of the blood are usually not much increased; rarely above 10,000. In the case reported in this paper they did not rise above 5200 per cmm. The differential count of the leukocytes has varied greatly. Planche and Lombard report 85 per cent. mononuclears in the blood of their case, while in our case there were 85 per cent. polymorphonuclear neutrophiles. The presence or absence of bronchopneumonia may have so great an influence on the blood picture that no definite conclusions can be drawn from these figures.

REPORT OF CASE. *Diagnosis: Typhoid fever (B. typhosus); purulent cerebrospinal meningitis; bronchopneumonia.*

The patient, I. J., a negress, aged nineteen years, was admitted to the medical service of the Johns Hopkins Hospital (Gen. No. 103845) on July 19, 1915. The patient was partially comatose when brought to the hospital. Her mother said that her daughter had been ill with typhoid fever for three weeks. Until the onset of this sickness the patient had never had any severe illness. For several days in the last week of June, 1915, she had had headache and dizziness. It was known on July 1 that she had fever, but she was not confined to bed until July 12, when she became prostrated and irrational. After that date a restless stupor supervened and the patient began to complain of headache and soreness in the neck.

On July 19 *physical examination* showed her to be a large, obese young negress, semicomatose, slightly jaundiced, and polypneic. Her temperature was 104° F.; pulse 132 per minute; respirations 40 per minute. The neck, slightly retracted, was painful when flexed, and Kernig's sign was slightly positive. The physical signs in the chest were those of bronchopneumonia of the lower lobes of both lungs. The abdomen was slightly distended and painful when palpated; the spleen could not be felt. The white blood cells were 5520 per cmm., with 83 per cent. polymorphonuclear leukocytes.

The signs of meningeal disease were so striking that a lumbar puncture was done at once. The spinal fluid appeared under normal pressure, was clear, watery, contained 6 cells per cmm., and gave a faintly positive globulin reaction by the Ross-Jones test. In the blood and spinal fluid the Wassermann reaction was negative, and the gold chloride reaction with the spinal fluid was normal. Cultures from the spinal fluid were negative.

On July 20 B. typhosus was grown from the blood culture and the Widal reaction was positive for the typhoid bacillus in dilution of 1 to 100. Throughout this day the patient's condition remained essentially unchanged. In the evening she became very stuporous, and a slight strabismus of the right eye appeared.

On July 21 she brightened mentally, but there was a definite divergent strabismus, slight rigidity of the neck, and absent patellar reflexes. She had been receiving ice-water sponges, and during this day her temperature did not rise above 102° F.

On July 22 her temperature rose rapidly to 103° F. She groaned continually in a restless stupor. At 10.30 P.M., with a temperature of 104° F., the white blood cells were 5200. At midnight, when her temperature was 106° F., she suddenly passed into clonic convulsions and became unconscious. There were violent jerking movements of all parts of the face, trunk, arms, and legs, and when the eyes were relatively still they showed a widely divergent strabismus. At this time her neck became readily flexible, the knee-jerks were elicited for the first time, and Kernig's sign was

no more positive than on her admission. After convulsions lasting for two hours the patient died. Lumbar puncture done during these agonal convulsions gave a turbid greenish-yellow spinal fluid under pressure of more than 200 mm. of water. The cells, not counted, formed a pavement of pus when spread on a microscopic slide. In stains for bacteria no organisms of any sort were discoverable. Cultures of the spinal fluid, however, yielded B. typhosus alone. This organism gave the typical cultural reactions of the typhoid bacillus and was agglutinated by a dilution of 1 to 3200 of the serum of a rabbit immunized with the laboratory's strain of B. typhosus. In making the cultures, varying amounts of the spinal fluid, were placed in several tubes of bile-broth and agar. Growth of the bacillus, however, occurred only in one tube. This, together, with the fact that no bacteria could be found in stained smears of the fluid, clearly indicates that very few bacilli were present, and suggests the manner in which the cause of an obscure case of meningitis might be overlooked.

Postmortem Examination. (No. 4410. Dr. R. Major. July 23, 1915.)

Summary of the Protocol. The subject was a large-framed, well-nourished negress, with slightly jaundiced conjunctivæ. Both pleural cavities were obliterated by dense fibrous adhesions. The lungs were extensively consolidated with areas of *bronchopneumonia.*

Intestine. The mucosa of the ileum near the ileocecal valve showed several round, raised, buttonhole-like ulcers, with necrotic material on their surfaces. The lymph follicles of the ileum and cecum were enlarged, and the mesenteric lymph nodes were large and soft.

Spleen. The spleen weighed 230 grams and showed the characteristic "acute splenic tumor" of infection. The liver weighed 1870 grams. The section of this organ showed extensive fatty change and areas of central necrosis. In the other organs, except the central nervous system, there were no significant abnormalities.

Brain. The meninges on the surface of the brain disclosed a considerable accumulation of yellowish-white creamy exudate. The greatest amount of this exudate was at the base of the brain, but along with the engorged bloodvessels, it continued upward over the convexity, fading out at the upper margins of the temporal lobes. The microscopic picture of this meningeal lesion corresponded with that described by MacCallum. In the arachnoid spaces and around the bloodvessels there were dense accumulations of polymorphonuclear cells. Near the pial vessels, penetrating the cortex, were a few large mononuclear cells, with inclusions in their cytoplasm, evidently the endothelial phagocytes described by MacCallum. The exudative process, however, did not affect the cortical substance of the brain. No bacteria were seen in this exudate.

SUMMARY. This report describes a case of purulent cerebrospinal meningitis due to B. typhosus, occurring in the fourth week of a typical case of typhoid fever. The outcome, as in similar cases, was lethal within a few days after the onset of the meningitis.

Statistics of the medical clinic of the Johns Hopkins Hospital show that out of 2768 cases of typhoid fever there have been 5 cases of typhoid meningitis. Seventeen case reports of this relatively rare phase of typhoid infection are summarized from the literature on the subject. These, together with the 15 cases collected by Cole, and with the case reported herein make a total of 33 proved accounts of the condition in the statistics of typhoid fever.

From these articles are collected comparative data on the spinal fluid in meningism, serous meningitis, and purulent meningitis.

Several cases of so-called "primary typhoid meningitis" are emphasized here, since lacking intestinal lesions, the mode of infection is obscure.

REFERENCES.

Achard, Ch. et Paisseau. Bull. et mém. Soc. méd. d. hôp. de Paris, 1904, xxi, 329.
Arzt, L., und Boese, J. Wien. klin. Wchnschr., 1908, xxi, 217.
Bramwell, E., Osler and McCrae. Modern Medicine, 1915, v, 167.
Claret et Lyon-Caen. Bull. et mém. Soc. méd. hôp. de Paris, 1909, xxviii, 217.
Cole, R. I. Johns Hopkins Hospital Reports, 1904, xii, 379.
Cruchet et Buard. Gaz. hebd. d. Soc. méd. de Bordeaux, 1902.
Delille, A. Pédicatrie pratique, 1905, iii, 89.
Gurd, F. B., and Nelles, T. B. Ann. Surg., 1908, xlviii, 4.
Hannes, B. Virchows Archiv f. path. Anat., 1914, ccxvi, 355.
Henry, J. N., and Rosenberger, R. C. AM. JOUR. MED. SC., 1908, cxxxv, 240.
Lavensen, R. S. Univ. Pennsylvania Med. Bull., 1908, xxi, 55.
Lemierre, A., et Joltrain, E. Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, xxxiv, 581.
Lessieur, C., et Marchand, M. J. Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, xxxiv, 780, 785.
MacCallum, W. G. Johns Hopkins Hospital Reports, 1904, 411.
McCrae, J. Lancet, London, 1905, i, 712.
Milligan, E. H. Brit. Med. Jour., 1908, i, 1295.
Netter. Bull. et mém. Soc. méd. d. hôp. de Paris, 1904, xxi, 332.
Nieter, A. München. med. Wchnschr., 1908, lv, 1009.
O'Carroll and Purser. Tr. Royal Acad. Med. of Ireland, 1912, xxx, 108.
Ortoconi, A., et Amenille, P. Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, xxxi, 187.
Planche et Lombard. Marseille-Médicale, 1914, li, 390, 456.
Raymond, F., et Siccard, J. A. Bull. et mém. Soc. mém. d. hôp. de Paris, 1905, xxii, 860.
Robinson, J. E. South Med. Jour., 1915, viii, 37.
Saquépée, E. Bull. et mém. Soc. méd. d. hôp. de Paris, 1910, xxx, 598.
Schütze, A. Berl. klin. Wchnschr., 1905, xlii, 1465.
Schwartz, B. Med. Rec., New York, 1910, lxxviii, 760.
Silberberg, L. Berl. klin. Wchnschr., 1908, xlv, 1354.
Southard, E. E., and Richards, E. T. Jour. Med. Research, 1908, xiv, 513.
Staübli, C. Deutsch. Arch. f. klin. Med., 1905, lxxxii, 90.
Stein, R. AM. JOUR. MED. SC., 1910, cxxxix, 542.
Stühmer, A. München. med. Wchnschr., 1911, lviii, 357.
Symmers, W. S., and Wilson, W. J. Jour. Path. and Bacteriol., 1909, xiii, 251

VISCERAL FINDINGS IN ONE HUNDRED SYPHILITICS.

By Tasker Howard,
BROOKLYN, N. Y.

Within the past few years our appreciation of the scope of syphilis as an etiological factor in visceral disease has been vastly widened. The routine application of the Wassermann reaction in the medical wards began immediately to direct our attention to the probability that this disease was responsible for many of the serious conditions in which it had previously been but vaguely suspected. The pathologists soon confirmed our suspicions by demonstrating the Treponema pallida in many of the suspected tissues and in some of the unsuspected. Coincidently they modified somewhat our ideas of the cellular pathology of the disease, or at least proved the syphilitic basis of certain pictures that had been considered of uncertain origin, as in the early myocardial changes of syphilis. Thus it has come about that syphilitic carditis, aortitis, pneumonitis, hepatitis, and so on have come to be comparatively common diagnoses in our medical wards.

These diagnoses are usually made, however, on very sick patients for whom far less can be accomplished than if the diagnosis had been made earlier. The source of supply of these patients seems to have received less study than the importance of the subject warrants, and the observations recorded here were made as a contribution to this phase of the subject. The syphilis clinics seemed to offer the best field for such a study, as the patients applying for treatement at these clinics usually do so because they know or suspect that they have syphilis, and not because of any suspicion that they have any visceral disease. This applies particularly to the early cases. The material in the syphilis wards at the Kings County Hospital and in the genito-urinary department of the Polhemus Memorial Clinic (Long Island College Hospital Dispensary) was kindly put at the disposal of the writer by the respective surgeons in charge, Dr. Winfield, Dr. Potter, and Dr. Fraser. I am much indebted to them and their staffs for many courtesies.

After some time spent in culling out interesting visceral lesions from this material it was decided to record also the negative findings. The work done was therefore discarded and the present series of 100 cases represents an unselected serial group in order that the frequency of the various findings might be indicated.

Of the 100 patients 22 were in the hospital, where it might be supposed that the more serious cases would be found; but as most of them merely came in for salvarsan they were not necessarily any worse than the 78 dispensary patients.

CLASSIFICATION. In order to compare the earlier with the later visceral manifestations the cases studied consisted in 50 in the secondary stage of syphilis and 50 later cases. Such a distinction is admittedly more or less artificial, but is nevertheless of some value in this connection. Patients were classified as in the secondary stage if they presented what are generally accepted as typical secondary external lesions or if they had been infected less than a year. As a matter of fact most of them were first seen as early untreated or almost untreated cases, and most of them were seen a number of times whether or not they presented pathological findings on the first examination. Patients were classified as in the tertiary stage if they presented no secondary lesions and had been infected for more than one year. The few mixed types encountered were classified as in the secondary stage. Patients in the tertiary stage were observed a number of times, so far as was possible, if they presented evidence of visceral disease. Otherwise they were not.

Eyes.—The pupils were unequal in 3 of the 50 secondary cases and in 7 of the tertiary cases. The Argyle-Robertson pupil was seen in no secondary case, but was found in 2 of the tertiary cases. They were both found to be suffering from tabes dorsalis. Exophthalmos was found in 2 early and 1 late case. All 3 were suffering from hyperthyroidism.

Thyroid Gland. Sixteen of the early and 14 of the late cases had thyroid glands which were visible and palpable. It should be stated that but two women were included in the entire series. The thyroid enlargement was well marked in 2 secondary and 1 tertiary case. It is very difficult to tell when a slight enlargement of the thyroid gland is pathological. I am quite ready to admit that the mere fact of its being visible and palpable is not proof that it is diseased, but the large proportion shown by the above figures leads one to suspect that syphilis had something to do with it. One would expect to find a larger proportion of enlarged thyroids among the earlier active than among the later ones. It can only be stated that the clinical impression gained was to the effect that the thyroids were more noticeably enlarged in the secondary cases. Measurements were not taken.

Hyperthyroidism was definitely established in 3 early and 3 late cases. In one of these the disease preceded the syphilis, but was augmented by it, and improved under antisyphilitic treatment. Of the 6 cases, 5 presented thyroid enlargement, 3 exophthalmos, 6 tachycardia, 6 fine tremor, 3 nervousness, 3 throbbing arteries; in 3 loss of weight was noticed. In a number of other patients the condition was suspected from the presence of various combinations of these symptoms, but was not considered definite enough to be included in such a statistical study. In 4 of the 6 patients the symptoms of hyperthyroidism were ameliorated by anti-

VISCERAL FINDINGS IN ONE HUNDRED SYPHILITICS.

By Tasker Howard,
BROOKLYN, N. Y.

Within the past few years our appreciation of the scope of syphilis as an etiological factor in visceral disease has been vastly widened. The routine application of the Wassermann reaction in the medical wards began immediately to direct our attention to the probability that this disease was responsible for many of the serious conditions in which it had previously been but vaguely suspected. The pathologists soon confirmed our suspicions by demonstrating the Treponema pallida in many of the suspected tissues and in some of the unsuspected. Coincidently they modified somewhat our ideas of the cellular pathology of the disease, or at least proved the syphilitic basis of certain pictures that had been considered of uncertain origin, as in the early myocardial changes of syphilis. Thus it has come about that syphilitic carditis, aortitis, pneumonitis, hepatitis, and so on have come to be comparatively common diagnoses in our medical wards.

These diagnoses are usually made, however, on very sick patients for whom far less can be accomplished than if the diagnosis had been made earlier. The source of supply of these patients seems to have received less study than the importance of the subject warrants, and the observations recorded here were made as a contribution to this phase of the subject. The syphilis clinics seemed to offer the best field for such a study, as the patients applying for treatement at these clinics usually do so because they know or suspect that they have syphilis, and not because of any suspicion that they have any visceral disease. This applies particularly to the early cases. The material in the syphilis wards at the Kings County Hospital and in the genito-urinary department of the Polhemus Memorial Clinic (Long Island College Hospital Dispensary) was kindly put at the disposal of the writer by the respective surgeons in charge, Dr. Winfield, Dr. Potter, and Dr. Fraser. I am much indebted to them and their staffs for many courtesies.

After some time spent in culling out interesting visceral lesions from this material it was decided to record also the negative findings. The work done was therefore discarded and the present series of 100 cases represents an unselected serial group in order that the frequency of the various findings might be indicated.

Of the 100 patients 22 were in the hospital, where it might be supposed that the more serious cases would be found; but as most of them merely came in for salvarsan they were not necessarily any worse than the 78 dispensary patients.

CLASSIFICATION. In order to compare the earlier with the later visceral manifestations the cases studied consisted in 50 in the secondary stage of syphilis and 50 later cases. Such a distinction is admittedly more or less artificial, but is nevertheless of some value in this connection. Patients were classified as in the secondary stage if they presented what are generally accepted as typical secondary external lesions or if they had been infected less than a year. As a matter of fact most of them were first seen as early untreated or almost untreated cases, and most of them were seen a number of times whether or not they presented pathological findings on the first examination. Patients were classified as in the tertiary stage if they presented no secondary lesions and had been infected for more than one year. The few mixed types encountered were classified as in the secondary stage. Patients in the tertiary stage were observed a number of times, so far as was possible, if they presented evidence of visceral disease. Otherwise they were not.

Eyes.—The pupils were unequal in 3 of the 50 secondary cases and in 7 of the tertiary cases. The Argyle-Robertson pupil was seen in no secondary case, but was found in 2 of the tertiary cases. They were both found to be suffering from tabes dorsalis. Exophthalmos was found in 2 early and 1 late case. All 3 were suffering from hyperthyroidism.

Thyroid Gland. Sixteen of the early and 14 of the late cases had thyroid glands which were visible and palpable. It should be stated that but two women were included in the entire series. The thyroid enlargement was well marked in 2 secondary and 1 tertiary case. It is very difficult to tell when a slight enlargement of the thyroid gland is pathological. I am quite ready to admit that the mere fact of its being visible and palpable is not proof that it is diseased, but the large proportion shown by the above figures leads one to suspect that syphilis had something to do with it. One would expect to find a larger proportion of enlarged thyroids among the earlier active than among the later ones. It can only be stated that the clinical impression gained was to the effect that the thyroids were more noticeably enlarged in the secondary cases. Measurements were not taken.

Hyperthyroidism was definitely established in 3 early and 3 late cases. In one of these the disease preceded the syphilis, but was augmented by it, and improved under antisyphilitic treatment. Of the 6 cases, 5 presented thyroid enlargement, 3 exophthalmos, 6 tachycardia, 6 fine tremor, 3 nervousness, 3 throbbing arteries; in 3 loss of weight was noticed. In a number of other patients the condition was suspected from the presence of various combinations of these symptoms, but was not considered definite enough to be included in such a statistical study. In 4 of the 6 patients the symptoms of hyperthyroidism were ameliorated by anti-

syphilitic treatment, the other 2 patients being lost sight of. The size of the thyroid was reduced in 2, the exophthalmos improved in 1 (with disappearance of v. Gräfe's sign), tachycardia in 4, throbbing vessels in 3, tremor in 1. Of the improved cases 2 were early and 2 were late. The writer has reported the case of a syphilitic woman with Graves's disease associated with transient hemolytic jaundice in which the four cardinal symptoms practically disappeared under antisyphilitic treatment.[1] Similar cures of syphilitic exophthalmic goitre have been recorded by Clark[2] and by Lewis.[3]

Lungs. No instance of syphilis of the lungs was recognized. Among the 50 early cases there were 5 who presented more or less definite evidence of pulmonary tuberculosis involving the apices. The stage of the syphilitic disease precluded a diagnosis of syphilitic pneumonitis. Considering the prevalence of phthisis it is not surprising that 5 out of 50 individuals suffering from an active debilitating infection, such as syphilis, should show signs of tuberculosis. That it was not found once among the tertiary cases suggests that those who had suffered from such a double infection had either succumbed earlier, or having passed the active stage of the syphilitic infection had overcome the other. Of the early cases seen none was of an advanced type, and none was watched long enough to determine whether the progress of the tuberculosis was unusually rapid. Among the tertiary cases there was one in whom there was definite dulness in the right back over the root of the lung, but lacking corroborative signs and symptoms a diagnosis of syphilis of the lung was not justified. There were 2 cases of emphysema in the older group.

Heart. It has been shown by Warthin[4] that the heart is a site of early predilection for invasion by the Treponema pallidum, and it is therefore not surprising there should be found considerable clinical evidence of cardiac involvement among the early as well as among the late cases. This subject has been emphasized in this country particularly by Brooks.[5] The most extensive statistical study is that of Grassmann,[6] who analyzed a series of 288 patients with secondary syphilis from the cardiac stand-point.

SUBJECTIVE SYMPTOMS. *Pain.* Of the secondary series there were 5 who complained of pain in the region of the heart or under the sternum. All 5 presented definite physical signs of abnormal cardiac conditions, which is in full agreement with Grassmann's observations on this point, the earlier observers having maintained that such symptoms were of purely functional origin.

[1] Med. Times, December, 1915.
[2] Jour. Am. Med. Assn., lxii, 1169.
[3] Ibid., lxi, 1630.
[4] AM. JOUR. MED. SC., May, 1914.
[5] Med. Record, February 24, 1912; New York State Jour. Med., June, 1913; Interstate Med. Jour., vol. xx, No. 6; AM. JOUR. MED. SC., cxlvi, 513.
[6] Deutsch. Arch. klin. Med., lxviii, 455 and lxix, 58.

Cardiac pain was present in 4 of the late cases, and in these also abnormal physical signs were present.

Palpitation. Eight of the early cases suffered from palpitation of the heart; 5 of these showed corresponding physical anomalies. The 3 who failed to show them were not suffering from the symptom at the time when they were examined but had previously complained of it, and had been under treatment for some months since that time. One third-stage patient who was suffering from hyperthyroidism complained of palpitation.

Dyspnea. Three early cases suffered from abnormal dyspnea on exertion. It was not a very marked feature in any of the cases in this series. However, the writer has seen three months after infection a severe myocardial breakdown, with marked dyspnea and edema. In this instance a recent debauche, to which the patient was unaccustomed, had acted as a contributory factor, but was obviously not the sole cause of the disturbance. His improvement after salvarsan was in striking contrast to his previous progress. Brooks[7] has reported similar myocardial failures in secondary syphilis. One late case, with broken compensation, suffered from dyspnea.

Edema was not seen except in the case last mentioned.

Physical Signs. *Arrhythmia.* The arrhythmia noted so frequently by most of the older writers in early syphilis was undoubtedly of the nervous type—the sinus arrhythmia. Of course, this bears no relation to cardiac integrity and is merely evidence of a hypersensitive nervous system. In this connection it is of some interest. Fifteen of the 50 early cases studied presented well-marked sinus arrhythmia as contrasted with the 2 of the 50 later cases who showed it. The inference is clear.

Extrasystoles, denoting a definite cardiac affection, were found but three times in the secondary series and once in the tertiary. It seems quite likely that many more examples would have been found if the time devoted to the examination of the pulse had been extended.

Auricular fibrillation was found in one late case.

Cardiac Enlargement. In studying the outlines of the heart, percussion findings were never accepted unless corroborated by palpation. A heart was not considered enlarged unless the apical impulse was definitely displaced. Enlarged hearts were found in 18 of the early cases and in 11 of the late cases.

Mitral Regurgitation. Mitral regurgitation, the presence of which could be recognized by its three cardinal symptoms, viz., apical displacement, typical murmur, and accentuated pulmonic second sound, was found in 8 early cases. Of the 8, 4 gave evidence of conditions other than syphilis which might account for

[7] Loc. cit.

it; 1 tertiary case had a leaking mitral. It is not presumed that in any instance there was present a syphilitic mitral endocarditis. The leaks were in all probability due to cardiac dilatation.

A systolic murmur at the apex, without other signs of regurgitation, was found in 11 early and 5 late cases.

A systolic murmur at the base was found in 11 early and 6 late cases. Aside from aortitis this murmur has about the same significance as the last mentioned.

A reduplication of the second sound, most typically discernible at the apex, was found in 7 of the early cases and in no late ones. This sign is usually associated with other evidences of myocardial involvement and seems to be rather characteristic of the condition.

Throbbing carotids were seen in 6 secondary and in no tertiary cases. The heart was described as overacting in 5 early and 1 late case.

Aortic regurgitation was conspicuous by its absence. Of course, syphilitic aortic regurgitation is a common condition, but its victims usually seek relief in some medical service.

Aortitis, as signified by a rough systolic murmur transmitted from the aortic area to the neck and by a ringing aortic second, was found in 1 early and 4 late cases. The early case was a man, aged twenty-three years, who has been infected six months. There was a widened area of supracardiac dulness beside the signs mentioned above. There was a slight general arteriosclerosis, no cardiac hypertrophy, and a blood-pressure of 118 to 85. He suffered from dyspnea but had no pain. He had never been sick before. Longcope[8] speaks of syphilitic aortitis occurring six and seven months after infection. Aneurysm of the aorta was found at autopsy in one late case in the hospital series. It was situated low down behind the heart.

Arteriosclerosis occurred in 4 early and 10 late cases. The early cases averaged twenty-seven years of age and the late cases thirty-eight years. It is impossible to hold syphilis responsible for all of these cases, but the figures are strikingly suggestive.

Blood-pressure readings were made in 20 early and 20 late cases. The early cases averaged 131 systolic and 84 diastolic, while the late cases averaged 137 systolic and 87 diastolic.

Summary of Heart Findings. Of the 50 syphilitic patients in the secondary stage, 24 (48 per cent.) gave definite evidence of cardiac pathology, not always of syphilitic origin, as has been seen. This does not include those presenting merely a sinus arrhythmia, an accidental murmur, an accentuated pulmonic second sound, or such inconclusive evidence of heart trouble, which probably accounts for the discrepancy observed in a comparison with Grassmann's

[8] Arch. Int. Med., January, 1913.

figures (77 per cent); 12 of the 50 late cases showed cardiac abnormalities. Many of these, however, merely represented the hypertrophy which accompanies an arteriosclerosis.

Effect of Treatment. Of the 14 cases of secondary syphilis with definite cardiac involvement, which were watched long enough to determine the effect of specific treatment, 11 showed improvement and 3 did not. The improvement usually amounted to a disappearance of all signs and symptoms. Possibly the 3 intractable cases would have shown improvement if watched over longer periods, although, of course, there are cases which fail to respond to all treatment.

The patients with tertiary syphilis presenting evidence of cardiac involvement, who were discovered in this investigation, for the most part presented no cardiac symptoms. The commoner physical signs, such as hypertrophy due to arteriosclerosis, would naturally not be affected by treatment, and these were not followed. One patient of the tertiary group with cardiac insufficiency had found so much relief from previous courses of antisyphilitic treatment that he had returned to the hospital a number of times, applying to the syphilitic department for treatment. The patient with aneurysm of the aorta died of bronchopneumonia shortly after admission. Only one of the patients with aortitis complained of symptoms, in this case pain, which was much relieved by salvarsan. Of the 4 patients in the tertiary stage who complained of cardiac pain, 2 were relieved by treatment and 2 were not.

Salvarsan Reaction. A peculiar cardiac reaction was twice noticed after the administration of salvarsan in early cases. This consisted in an augmentation of the signs of cardiac involvement or their appearance, such as might represent a Herxheimer reaction, except for the fact that the disturbance lasted for from two to three weeks. There was evident dilatation in both cases. A repetition of the dose was not followed by a similar reaction. This phenomena has also been noted in patients not included in this series. If the dilatation were an arsenic reaction one would expect that the individual would show the same reaction to later doses of the drug. It seems more likely that it is a true Herxheimer reaction and that the heart takes longer to recover its normal condition than do other tissues. I believe it is important that the heart should be carefully watched after the administration of salvarsan, and any signs of dilatation of the heart should be considered indications for absolute rest as long as such signs persist.

Kidneys. The kidneys were not investigated as thoroughly as they might have been. Of the secondary cases, urinalyses were made in 15 instances and albumin found in 2. One of these, an early case, was admitted to the hospital with an acute nephritis and typical secondary symptoms. He had received four intramuscular injections of mercury. The relation of the syphilis to the

nephritis is problematical. Of the later cases the urine was studied in 8 and was negative in all.

Suprarenals. One case of Addison's disease of syphilitic origin was practically cured by antiluetic treatment, and has been reported by the writer and Dr. Schaffner.[9]

Digestive Disturbances. Digestive disturbances were of rare occurrence. But one of the secondary cases complained of any indigestion which had appeared since the infection, and that amounted merely to a tendency to constipation and flatulency. Of the tertiary cases 2 complained of slight indigestion and 1 of symptoms of gastric ulcer. This patient left before treatment could be properly instituted. Among the tertiary cases there were 3 with serious stomach symptoms, and these all proved to be the gastric crises of tabes.

The Liver. In spite of the fact that the liver comes after the testicle and brain in frequency of involvement (according to Brooks[10]), the clinical manifestations of hepatic involvement are by no means as frequent as are those of other organs. This Brooks ascribes to the large margin of safety which the liver possesses. It is said that jaundice occurs in 1 to 2 per cent. of secondary cases.[11] This is probably due to the invasion of the liver by the spirochetes,[12] although it is sometimes considered toxic in origin. Brooks has demonstrated obstruction of the biliary radicles through pressure from adjacent syphilitic periarteritis. In the present series 1 of the 50 secondary cases presented slight jaundice with an enlarged and tender liver, and in 2 other patients the liver was palpable. Of the tertiary cases the liver in 1 was 2 inches below the costal margin when first seen and had disappeared after two months' treatment. In 2 others of this series the liver was palpable, 1 having a ptosed liver and 1 cardiac disease with broken compensation.

Spleen. In only 2 cases of secondary syphilis was there demonstrable enlargement of the spleen, and 1 of these gave a history of malaria. These findings are radically different from those of Wile and Elliott,[13] who noted enlarged spleens in 36 per cent. of their cases. Other authors whom they quote give figures varying from about 2 per cent. to 10 per cent. The writer has found enlarged spleens in several cases of secondary syphilis not included in this series, but in nothing like the proportion noted by Wile and Elliott. In the tertiary group an enlarged spleen was found in one patient who gave a history of malaria.

[9] New York Med. Jour., May 27, 1916.
[10] Ibid., June 27, 1914.
[11] Editorial, Jour. Am. Med. Assn., lxi, 1633.
[12] Brooks: Loc. cit.
[13] Am. Jour. Med. Sc., cl, 512.

Nervous System. In the early cases some degree of mental perturbation and nervous hypersusceptibility was, of course, the rule. This was demonstrated physically by the frequency of nervous cardiac arrhythmias (30 per cent.). No case of definite syphilitic involvement of the nervous system was found.

In the tertiary group there was 1 case of transverse myelitis which occurred one year after infection (hospital case) and 3 cases of tabes, beside a palatal palsy of peripheral origin and a hemiplegia in a man, aged thirty-one years, coming on three years after infection.

Joints. The frequency of the occurrence of syphilitic arthropathies has been recently emphasized by Higgins.[14] In the present series 1 patient in the secondary group gave a history of pain and swelling of the fingers and knees at the same time that he was suffering from sore throat and mucous patches. All of the symptoms had disappeared during the four weeks of antisyphilitic treatment he had received at the dispensary before he was seen by the writer.

Conclusions. Visceral syphilis is at least as common and much more serious than cutaneous syphilis, which has in times past been given the greater amount of attention. The manifestations of visceral syphilis are detectable in the early stages of the disease in a large proportion of cases. Such manifestations are about as readily controlled by proper treatment as are the visible signs of the disease. It is important, however, in view of the extreme seriousness of the later stages of visceral syphilis, that the treatment be pushed energetically from the start in order to eradicate the disease while it is possible and before irremediable damage has been done. Furthermore, it is important that every patient with syphilis be carefully watched for signs of such visceral involvement as should indicate treatment beside the ordinary antisyphilitic measures. For example a dilatating heart in early syphilis indicates rest just as clearly as though it were due to rheumatic carditis, and the neglect of this precaution may leave the patient with a weak heart even though he be lucky enough to be cured of his syphilis.

Cardiac dilatation of several weeks' duration sometimes occurs after the administration of salvarsan.

To sum up, our medical wards will be deprived of their present generous supply of syphilitic wrecks only when every syphilitic patient is treated early, thoroughly, persistently, and with painstaking consideration of his individual requirements.

[14] Am. Jour. Med. Sc., cl, 733.

PULSATING SPLEEN IN MITRAL AND TRICUSPID DISEASES.[1]

By Morris Manges, M.D.,

PROFESSOR OF CLINICAL MEDICINE, UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE; VISITING PHYSICIAN, MOUNT SINAI HOSPITAL, NEW YORK.

S. S., aged sixteen years, entered Mt. Sinai Hospital in November, 1910. She had been in the hospital one and a half years before on account of chronic endocarditis, and double mitral disease with auricular fibrillation, which was rheumatic in origin.

At that time it was noted that the liver was tender and pulsating, and that the spleen was also large and tender. She left the hospital much improved; but one month later the old symptoms came back, and since then there had been more or less loss of compensation, on account of which she reëntered the hospital.

The physical status was that of advanced double mitral lesions, with tricuspid regurgitation and a moderate dilatation of both ventricles. There was also a short localized diastolic murmur over the third space to the left of the sternum. An effusion in the right chest reached the angle of the scapula. The liver extended to the umbilicus; it was hard, nodular, tender, and pulsating. The spleen was also enlarged upward and downward, and almost extended to the umbilicus. It was hard and nodular; at the tip there was a large, firm nodule. The spleen reached almost as far as the liver, but it did not touch it, as a distinct space was felt between the two organs. No note was made of pulsation of the spleen at the time of admission.

The radial pulse was small, rapid, and irregular. The veins in the neck pulsated forcibly. The polygraph showed auricular fibrillation. Systolic blood-pressure was 110 to 115.

The blood count showed 6,700,000 to 8,000,000 red blood cells; 9000 to 13,000 white blood cells; 90 per cent. polynuclears; hemoglobin 84 per cent. The urine showed a heavy trace of albumin and many granular casts.

The peculiar feel of the liver and spleen led me to suspect syphilis, although no history of it could be obtained. The Wassermann reaction was strongly positive.

It was not until the patient had been in the hospital two weeks that the pulsation was observed in the spleen for the first time. It was probably present at the time of her admission, but it was not observed. It persisted throughout her stay in the hospital. It was a distinct expansible pulsation, which was best observed on bimanual palpation, its time usually preceding that of the liver, but sometimes it seemed to coincide with it.

The course of the disease was that of any ordinary advanced

[1] Read at the meeting of the American Climatological and Clinical Association, Washington, May 10, 1916.

endocarditis, with an occasional infarct. She was in the hospital for a long time, and she left much improved, although when she left the fibrillation of the auricle and the pulsation of the liver and spleen were still present. Although efforts were made to trace her, she was never heard from again. This report has been delayed in the hope of observing the case again and also in the expectation of observing additional cases of pulsating spleen. However, in spite of systematic routine palpation of every enlarged spleen during the past six years I have been unable to find any additional cases.

It is to this feature of this case to which I would call attention, since this is a symptom of very rare occurrence. It was first described by Tulpius[2] in 1652. Gerhardt,[3] in 1882, reported a case in a man who had an old aortic regurgitation, and who also had malarial fever. Later on, Gerhardt[4] was also able to report two additional cases of aortic regurgitation, in both of which pericarditis with fever developed during their stay in the hospital. In both of these patients he discovered pulsation of the spleen during the febrile stage of the disease. He also noted that the increase in the size of the spleen was much greater than was usually observed under such conditions.

Prior[5] reported two cases. The first case was that of a well-compensated aortic regurgitation in which typhoid fever was contracted. The spleen only pulsated during the course of the fever. The second case was one of hypertrophy of the left ventricle, which was the result of overexertion in a workman, aged thirty-seven years. Pulsation of the spleen occurred during the course of an attack of croupous pneumonia.

Drasche[6] reported a case of pulsating splenic tumor in a female, aged seventeen years, with an advanced aortic regurgitation which had appeared during the febrile stage of an attack of croupous pneumonia. The enlarged pulsating spleen disappeared as soon as the fever was gone.

To these cases which have been collected by Litten[7] I have been able to add two additional cases, both observed by Gerhardt;[8] both of these men had aortic regurgitation and developed the pulsation of the spleen during attacks of lead colic; in both patients the pulsation disappeared as soon as the attack of lead colic was over. Fever was present in one patient and was absent in the other. In the former the liver also pulsated. No reference was made to the liver in the latter case.

[2] Quoted by Litten: Loc. cit. (7).
[3] Ztschr. f. klin. Med., 1882, Band iv, 449.
[4] Charité Annalen, 1887, Band xxii, 229.
[5] München. med. Wchnschr., 1887, Band xxxiv, 669.
[6] Wiener med. Blätter, 1888, Band xi, 1.
[7] Nothnagel's Spec. Pathol. u. Therap., 1898, Band viii, Theil 2, p. 75.
[8] Centralbl. f. klin. Med., 1888, Band ix, 1.

With the exception of the historic case of Tulpius, which he observed in 1652, all of these cases were observed within the period from 1882 to 1888. I have been unable to find any cases after this date; a striking commentary on how the careful clinical examinations have been lost since the laboratory has played such a preponderating role in the making of diagnoses.

In all of these cases the splenic pulsation was arterial and was synchronous with the cardiac systole and increased and diminished with the vigor of the cardiac action. Prior's 2 cases showed this very strikingly; in the pneumonia patient the pulsation seemed very much less during the period of cardiac weakness; and it also almost disappeared as soon as the spleen decreased in size when the fever was gone. In the 2 cases of lead colic it was only present during the period of very high blood-pressure associated with the colic.

According to Gerhardt and Litten three factors are needed: an enlarged spleen, chronic cardiac disease, and an acute febrile disease. The chronic cardiac disease always represented a marked hypertrophy of the left ventricle, usually with aortic regurgitation; only once was there idiopathic hypertrophy of the left ventricle. The fevers included pneumonia, malaria, and typhoid fever. Litten explains the phenomenon as being the result of the fever increasing the vascularity of the spleen and relaxing its tissue. As a result, the pulsation of the arteries is transmitted more readily and distinctly through the organ. This explanation does not hold in the 2 cases of lead colic. Here Gerhardt assumes that a high blood-pressure associated with the lead colic makes the pulsation in the splenic vessels more forcible.

The present case differs from those thus far reported. There was no evidence of aortic regurgitation, unless the short diastolic murmur in the third left space might be accepted as evidence of aortic regurgitation, of which, however, there was no other symptom, and there was no Corrigan pulse or double tone in the vessels; the tracings showed no sign of it; the hypertrophy of the left ventricle could easily be explained by the mitral lesion.

How can it be explained? Surely not according to Gerhardt and Litten, for most of the conditions postulated by them are absent; there was neither fever nor acute infectious disease, and there was no aortic regurgitation. There was an hypertrophy of the left ventricle and there was an enlarged spleen. The hypertrophy of the left ventricle was mitral in origin; the splenic enlargement was partly due to the cardiac disease and partly to the syphilis. There was no evidence of aneurysm or any pulsating vascular tumor.

The question at once arises whether the pulsation may not have been transmitted from the heart, liver, or aorta. This may be dismissed because the pulsation was distinctly expansile and independent of any of the other viscus. This could readily be demonstrated on bimanual examination. There were no pulsating tumors

or cysts of the spleen, and the pulsation must have originated in the splenic vessels. This was well illustrated by a series of tracings which was made by Dr. Alfred E. Cohn. The tracings include the time relations of the spleen to the liver, cardiac apex, and radial and femoral arteries. These tracings were studied by Dr. Cohn and Dr. B. S. Oppenheimer. It is not an easy task to draw con-

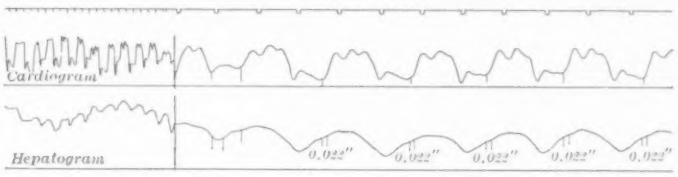


FIG. 1.—Tracings of heart and liver.

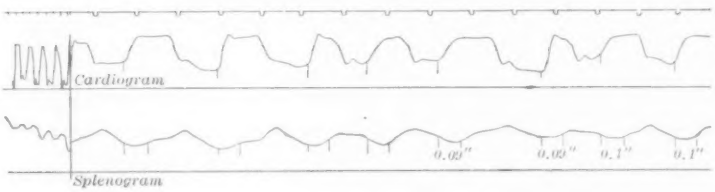


FIG. 2.—Tracings of heart and spleen.

FIG. 3.—Tracings of heart and femoral artery.

clusions from them, as unfortunately no jugular or abdominal aorta tracings were made. Dr. Cohn was inclined to regard the splenic pulsations as arterial. The pulsations in the liver he considers to be of the ordinary ventricular type. Dr. Oppenheimer, after a very careful study of the tracings, is unable to reach any positive conclusions concerning the nature of the splenic tracings. He agrees

with Dr. Cohn in considering the liver pulsations to be ventricular. When two observers who have had such a large experience in interpreting tracings are unable to agree, I believe it will be wisest to simply state the findings and to leave their exact determination to the future, when possibly more cases will have been observed. The following are the time relations:

1. The cardiohepatic time is 0.022 second (Fig. 1).
2. The cardiosplenic time is 0.09 or 0.1 second (Fig. 2).
3. The cardiofemoral time is 0.1 second (Fig. 3).

These figures would indicate that the splenic pulsations are arterial, as the time relation of the femoral artery agrees so closely with that of the spleen. The dynamic conditions which exist in this case, however, do not warrant this assumption, as this conclusion would predicate the existence of an aortic regurgitation, of which there are almost no evidences. The only possible warrant for it is the short diastolic murmur in the third left space. This is not enough for a diagnosis of aortic regurgitation, all the evidence of which was absolutely lacking, although it was carefully sought for during the long period she was under observation. But even if we did assume it to be present, all the other postulates of Gerhardt and Litten are absent. To assume that the pulsation in the spleen is arterial and that that in the liver is venous is an improbable assumption. The most plausible explanation is to attribute both pulsations in the liver and the spleen to the same source, *i. e.*, venous, for this is the type usually seen in tricuspid regurgitation. This, too, is improbable, for it is inconceivable that the propagation of the pulsations in the liver which is so closely related to the inferior vena cava should also be propagated into the splenic vein, which is a branch of the portal vein.

It is greatly to be regretted that I cannot offer any explanation of this unique case. Unfortunately, it is the only case of the kind which has ever been reported, and it was observed six years ago, when the new cardiographic methods were still in their infancy.

THE RATE OF EXCRETION OF THE THREE NITROGENOUS WASTE PRODUCTS, URIC ACID, UREA AND CREATININ IN NEPHRITIS, AS SHOWN BY COMPARATIVE STUDIES OF THE BLOOD AND URINE.

By C. K. Watanabe, M.D.,

NEW YORK.

(From the Laboratory of Pathological Chemistry, New York Post-Graduate Medical School and Hospital.)

The accumulation of the end products of protein metabolism in conditions of renal insufficiency is now a well-established fact.

Recent work in this laboratory[1] has shown that as the permeability of the kidney is lowered, this becomes evident: (1) by a retention of uric acid, (2) by that of urea, and (3) by that of creatinin, indicating that creatinin is the most readily eliminated of these three nitrogenous waste products and uric acid the most difficulty eliminated, with urea standing in an intermediate position. To obtain more definite information on this point, it has been thought worth while to compare the concentration of these waste products in the blood with their elimination in the urine. The blood and urine have, accordingly, been studied in a number of miscellaneous cases of nephritis, and likewise, for comparison, in a few individuals free from kidney disease.

A comparatively large amount of work has been done in which simultaneous determination of blood and urine urea have been made but no work of a similar nature has been carried out with uric acid and creatinin. Considerable interest was aroused in the mechanism of the excretion of urea, following the work of Ambard and Weill[2] upon the relationship between the blood urea and the rate of urea excretion. In this country McLean and Selling,[3] McLean,[4] and Addis and Watanabe[5] have reported a large number of observations dealing with this subject.

Methods Employed. The technic employed in the collection of specimens was almost identical with that of McLean.[6] After seventeen hours' starving, about 200 c.c. of water was given, and one and one-half hours later the collection of urine was started and a seventy-two-minute specimen collected. In patients in whom an incomplete urination was anticipated, the bladder was emptied with a catheter at the beginning and at the end of the period. In the middle of the period of urine collection, 20 c.c. or over of blood were taken.

For the estimation of the urea of both blood and urine, Van Slyke and Cullen's[7] modification of Marshall's method was employed. The Folin and Denis-Benedict[8] method for uric acid in the blood was carried out as described by Myers and Fine,[9] while for the urine the exact technic given by Benedict and Hitchcock[10] was followed. Folin's methods were used for the creatinin of both blood[11] and urine.[12]

[1] Myers, V. C., Fine, M. S., and Lough, W. G.: The Significance of the Uric Acid, Urea and Creatinin of the Blood in Nephritis, Arch. Int. Med., 1916, xvii, 570.
[2] Jour. physiol. et path. gen., 1912, xiv, 753.
[3] Jour. Biol. Chem., 1914, xix, 31.
[4] Jour. Exper. Med., 1915, xxii, 212 and 366; Jour. Am. Med. Assn., 1916, lxvi, 415.
[5] Jour. Biol. Chem., 1916, xxiv, 203; 1916, xxvii, 249.
[6] Loc. cit.
[7] Jour. Biol. Chem., 1914, xix, 211.
[8] Ibid., 1915, xx, 619.
[9] Loc. cit.
[10] Loc. cit.
[11] Folin, O.: Jour. Biol. Chem., 1914, xvii, 475.
[12] Folin, O.: Am. Jour. Physiol. 1915, xiii, 48.

TABLE I.—COMPARATIVE DATA ON THE BLOOD AND URINE IN 25 CASES.

Case.	Date, 1916.	Age.	Sex.	Blood analyses. Mg. to 100 c.c.			Relationship between the concentration in the blood and rate of excretion. Mg. per 100 c.c. blood divided by mg. excreted per 1 hour.			Index of urea excretion (McLean).	Diagnostic remarks.
				Uric acid.	Urea.	Creatinin.	Uric acid	Urea.	Creatinin.		
1-M. N.	June 20	46	M	9.2	258	9.4	2.20	2.00	0.70	0.2	Chronic interstitial nephritis; uremia. Died.
	June 23			9.1	336	9.3	....	....	....	...	
	June 27			9.1	348	10.0	1.90	1.10	0.54	3.2	
	June 30			10.0	442	12.5	1.63	1.42	2.00	0.1	
2-W. W.	June 9	30	M	4.2	145	9.6	....	0.43	....	1.3	Chronic interstitial nephritis; uremia.
3-M. C.	July 7	11	M	6.3	129	2.8	1.29	1.29	0.33	1.2	Acute parenchymatous nephritis. Improved.
	July 28			6.8	107	2.3	0.82	0.32	0.08	6.2	
	Aug. 8			7.2	93	3.9	1.10	0.32	0.13	6.5	
4-L. R.	July 18	25	F	6.0	122	10.0	1.46	2.63	1.28	0.3	Acute parenchymatous nephritis; uremia. Died.
5-J. Fi.	July 17	60	M	5.3	77	3.1	0.12	0.04	0.05	68.0	Chronic endocarditis.
	July 24			4.4	60	2.3	....	....	....	...	
6-G. A.	Aug. 18	43	M	5.5	56	3.5	0.15	0.07	0.08	42.0	Leukemia.
7-V. D.	July 11	36	M	9.3	39	2.6	0.39	0.04	0.06	77.0	Cardiac insufficiency.
	July 17			8.9	52	2.7	0.64	0.14	0.08	20.0	
	July 24			5.0	49	2.1	0.37	0.13	0.09	26.0	
	Aug. 4			6.1	40	2.1	0.47	0.12	0.09	33.0	
	Aug. 11			6.7	40	1.8	0.58	0.12	0.06	35.0	
8-E. N.	July 11	50	F	7.1	50	3.1	1.10	0.23	0.19	08.0	Probable gout; chronic endocarditis.
9-A. M.	June 23	63	M	5.4	29	2.4	0.20	0.05	0.10	75.0	Chronic interstitial nephritis; syphilitic adenitis.
	June 27			4.5	37	2.7	....	....	....	...	
	June 30			7.7	48	2.1	0.32	0.10	0.12	35.0	
	July 7			5.0	...	2.9	0.24	....	0.10	...	
	July 14			4.4	42	3.3	....	....	....	...	
10-E. P.	June 23	50	M	5.0	42	2.3	0.28	0.07	0.03	31.0	Probable hypernephroma.

11–J. F.	July 7	40	M	6.1	39	2.9	0.47	0.11	0.14	54.0	Aortic regurgitation; hypertention.
	July 20			6.3	29	2.8	0.93	0.10	0.15	35.0	
	Aug. 1			4.6	32	2.0	0.37	0.10	0.06	65.0	
12–S. H.	Aug. 18	38	F	4.0	39	3.3	0.27	0.06	0.10	90.0	Chronic interstitial nephritis; hypertention.
13–M. R.	July 20	49	M	6.4	38	3.0	0.19	0.02	0.04	168.0	Endocarditis; myocarditis; chronic interstitial nephritis.
	Aug. 1			4.6	24	2.2	0.17	0.04	0.03	99.0	
	Aug. 8			6.3	35	3.9	0.24	0.04	0.05	55.0	
	Aug. 18			6.0	32	2.9	0.29	0.08	0.04	42.0	
	Sept. 1			5.8	32	1.8	0.26	0.08	0.02	45.0	
14–J. O.	June 20	54	M	10.0	30	2.2	0.72	0.10	0.06	68.0	Mania.
15–F. R.	June 30	22	M	5.1	27	2.3	0.21	0.06	0.05	75.0	Chronic interstitial nephritis; syphilitic adenitis.
	July 7			3.3	15	3.1	0.06	0.03	0.07	250.0	
	July 14			4.0	28	3.9	0.12	0.05	0.08	82.0	
	July 28			4.5	27	1.9	0.26	0.04	0.05	110.0	
	Aug. 8			5.6	25	4.0	0.27	0.07	0.09	74.0	
16–F. B.	Aug. 18	39	M	6.3	27	2.1	0.30	0.05	0.04	70.0	Syphilis.
17–H. B.	July 14	49	M	2.6	17	3.6	0.09	0.02	0.08	377.0	Endarteritis obliterans; arteriosclerosis.
	July 20			3.7	24	3.7	0.35	0.09	0.10	79.0	
	July 28			3.6	24	3.6	0.12	0.04	0.08	101.0	
18–S. J.	July 26	63	F	5.3	24	4.2	0.09	0.02	0.05	248.0	Chronic diffuse myocarditis; asthma.
19–R. V.	Aug. 25	60	M	4.6	23	1.5	0.16	0.07	0.05	102.0	Gastric ulcer; arteriosclerosis.
20–H. H.	Aug. 11	31	M	...	36	1.7	....	0.02	0.02	220.0	Duodenal ulcer; chronic appendicitis; constipation.
21–P. J.	July 11	60	M	4.0	29	2.3	0.18	0.07	0.07	64.0	Emphysema; bronchitis.
	July 17			3.8	33	2.4	0.15	0.07	0.08	68.0	
	July 24			3.8	33	2.2	0.15	0.04	0.05	20.0	
	Aug. 4			...	33	1.3	....	0.05	0.03	74.0	
22–M. D.	Aug. 11	29	M	4.0	30	2.0	0.31	0.09	0.05	70.0	Gastric ulcer.
23–H. A.	Aug. 25	25	M	4.5	30	1.7	0.10	0.05	0.04	107.0	Sciatic neuritis; neuralgia.
24–W. N.	June 13	24	M	4.8	26	2.4	0.26	0.03	0.04	90.0	Probable gonorrheal arthritis.
	June 20			3.8	30	2.1	0.25	0.04	0.03	79.0	
25–J. K.	Aug. 8	62	M	2.5	18	2.5	....	....	....	...	Carcinoma of pylorus.
	Aug. 11			1.8	21	2.2	0.32	0.08	0.07	102.0	

Ambard and Weill,[13] McLean and Selling,[14] and McLean[15] have endeavored to show that there is a constant relationship between the urea of the blood and urine when simultaneously determined under certain uniform time conditions. They have worked out formulæ for the relationship of the blood urea to the urine urea, and state that the resultant of these formulæ, *i. e.*, the combined formula (Ambard and Weill) and the index of urea excretion (McLean), is relatively constant for normal individuals, but that deviations exist in proportion to the renal insufficiency. These conclusions are not in entire harmony with our own observations, as will be pointed out at another time.

In the present paper we wish to discuss the comparative relationship of the urea, uric acid, and creatinin of both blood and urine. Fifty-five observations are recorded in 25 cases in which such determinations were simultaneously carried out, the urine specimens being collected for seventy-two minutes (one-twentieth of the twenty-four hours, as in McLean's experiments). There was some evidence of nephritis in the first 19 cases of this series, the order of arrangement being according to the descending magnitude of the blood urea. The remaining 6 cases were not regarded as cases of nephritis, and are included for purposes of comparison.

From an inspection of the blood analyses in Table I, it will be noted that there was marked nitrogen retention in the first 4 cases, 2 of the cases being diagnosed as chronic interstitial nephritis and 2 as acute parenchymatous nephritis. Case 5, suffering from chronic endocarditis, showed a blood urea quite above the normal limits, while the blood ureas of Cases 6 to 12 were likewise rather above the figures usually encountered in hospital cases not suffering from an impairment in renal function.

TABLE II.—AVERAGE COMPOSITION OF THE BLOOD FOR GROUPS OF CASES.[16]

Cases.	Impairment of renal Function.	Uric acid.	Urea.	Creatinin.
		mg. to 100 c.c. of blood.		
1 to 4	Severe	7.5	220	7.7
5 to 14	Moderate	6.0	41	2.6
15 to 19	Slight	4.4	24	3.1
20 to 25	Very slight (?)	3.7	29	2.1

A general idea of the variations found in the nitrogenous waste products of the blood in the different cases may be obtained from the average data given in Table II. It will be noted that for the average

[13] Loc. cit. [14] Loc. cit. [15] Loc. cit.

[16] Normal blood findings: Uric acid 2 or 3 mg., urea 25 to 35 mg., and creatinin 1 to 2.5 mg. all calculated per 100 c.c. of blood. The above figures for the normal urea of the blood refer primarily to hospital patients on a low protein diet.

data on Cases 1 to 4 the figures for all three waste products are high, although in comparison with the other cases this is especially marked for the urea and creatinin. In the second group of cases (5 to 14) it will be noted, on the other hand, that the retention is most marked in the case of the uric acid and least so in the case of the creatinin. The observations in these two groups of cases corroborate the findings of Myers, Fine and Lough. In the third group of cases (15 to 19) the figure for urea is normal, but there is an appreciable retention of both uric acid and creatinin. According to the view we have held, this would not be surprising so far as the uric acid is concerned. It is worthy of note that we have frequently found that a slight retention of creatinin occurs in syphilis, certain heart conditions, and in some advanced cases of diabetes. The figures in the fourth group of cases (20 to 25) are perfectly normal, except for a slight retention of uric acid.

A ratio has been worked out to show the relationship between these waste products in the blood and urine by dividing the milligrams of the substance per 100 c.c. of blood by the milligrams excreted per hour. From these ratios (Table I) it is evident that uric acid is much less readily eliminated than either urea or creatinin. For the urea and creatinin there is comparatively little difference, although on the average creatinin seems to be slightly more readily eliminated. This harmonizes very well with the conclusions from the determinations in the blood alone. The solubility of uric acid, even as sodium or potassium urate, is very much less than that of the urea or creatinin, and this may be the important factor in the comparatively low permeability of the kidney for this substance.

It is interesting to note in Case 1 that although uric acid was the least readily eliminated of the three waste products on the first examination, creatinin was the most poorly excreted just before death. In Case 4 it will further be observed that the urea was the most poorly eliminated.

It is believed that a general idea of this topic can best be obtained by a summary table of average figures similar to that employed in the case of the blood analyses. Such data have been collected in Table III.

TABLE III.—AVERAGE DATA ON THE RELATIONSHIP OF THE URIC ACID, UREA AND CREATININ OF BLOOD AND URINE.

Cases.	Relationship between the concentration of the nitrogenous waste products in the blood and the rate of their excretion. Mg. per 100 c.c. blood divided by mg. excreted per one hour.			Index of urea excretion (McLean).
	Uric acid.	Urea.	Creatinin.	
1 to 4	1.49	1.190	0.721	2.4
5 to 14	0.40	0.088	0.079	55.8
15 to 19	0.18	0.050	0.068	142.4
20 to 25	0.21	0.054	0.047	99.3

It will be noted that with the exception of the first group of cases (1 to 4) the uric acid was from three to four times less readily eliminated than the urea or creatinin. A comparison of the data in Groups 1, 2 and 4 would seem to substantiate the view that as the permeability of the kidney was lowered this was evident first by a retention of uric acid, later by that of urea and lastly by that of creatinin.

Ambard and Weill[17] attempted to estimate the functional ability of the kidney in normal and pathological conditions by a study of the ratio between the urea of the blood and urine. They state that they found a relatively constant ratio in normal individuals, and conclude that a deviation from this normal shows a deficiency in the function of the kidney. McLean[18] modified the formula so that the normal of his so-called "index of urea excretion" would be 100. He believed that indices below 80 showed some deficiency in the function of the kidney. The formulæ that have been used to show this relationship are given below:

Ambard's First Formula:

$$\frac{\text{Gm. of urea per liter of blood}}{\sqrt{\text{Hourly rate of excretion} \times 24 \times \frac{70}{\text{Kg. of body wt.}}}} = \text{K.}$$

Ambard's Second Formula:

$$\text{Hourly rate of excretion} \times 24 \times \frac{70}{\text{Kg. of body wt.}} \times \sqrt{\text{Gm. of urea per liter of urine}} = \text{K.}$$

Combined Formula:

$$\frac{\text{Gm. of urea per liter of blood}}{\sqrt{\frac{\text{Gm. of urea per 24 hrs.}}{\text{Kg. of body wt.}} \times \frac{70}{25} \times \text{Gm. of urea per liter of urine}}} = \text{K.}$$

McLean's Index:

$$\frac{\text{Gm. of urea per 24 hrs.} \times \sqrt{\text{Gm. of urea per liter of urine}} \times 8.96}{\text{Body wt. in kg.} \times (\text{Gm. of urea per liter of blood})} = 100.$$

From a large number of observations made on normal individuals using the first and second formulæ of Ambard, Addis and Watanabe[19] conclude that the rate of urea excretion in man varies under physiological conditions in a manner which cannot be explained by the concentrations of urea in the blood and urine. They observed that there was a tendency to an increased rate of urea excretion to exist with higher blood urea concentrations in certain conditions in normal individuals, and that in cases with a deficiency in kidney function, there was a lowered rate of urea excretion even in the presence of a higher blood concentration. The results of Addis and Watanabe are summarized in Table IV.

[17] Loc. cit. [18] Loc. cit. [19] Loc. cit.

TABLE IV.—VARIATIONS FOUND BY ADDIS AND WATANABE[20] FOR THE RELATION BETWEEN THE UREA OF THE BLOOD AND URINE IN NORMAL INDIVIDUALS.

	Ambard's first formula.[21]	Ambard's second formula.[23]	Combined formula.[23]	McLean's index.[22]
Lowest . .	0.0451	27.9	0.0451	23.2
Highest .	0.1430	570.0	0.1430	355.0
Average .	0.0762	117.2	0.0762	99.6

The results obtained show such marked variations, both normally and pathologically, that it is believed that they are of comparatively little more value, either for diagnostic or prognostic purposes, than the blood urea alone.[24]

An inspection of the average data for the McLean index, given in Table III, shows that these average figures fit in very nicely with the other data. If we examine the observations as given in Table I more carefully, however, the actual practical value of the index will be found to be very small. Very low indices were found in Cases 3 and 8, but the blood creatinin was a far more reliable prognostic sign, and the same was true of Cases 7, 9, 10 and 11, with comparatively low indices.

CONCLUSIONS. From a comparative study of both blood and urine it is evident that uric acid is normally much less readily eliminated than either urea or creatinin. Although creatinin seems to be excreted slightly more readily than urea under normal conditions, there would appear to be comparatively little difference in the ability of the kidney to eliminate these two waste products.

With a lowering in the activity of the kidney the uric acid is apparently the first to suffer, although in advanced stages of nephritis the ratio between the urea of the blood and urine may be even higher than the uric acid. In these severe cases, creatinin would quite uniformly seem to be the last to be markedly influenced.

The combined formulæ of Ambard and Weill or the index of urea excretion of McLean give little more information of diagnostic or prognostic value than the blood urea alone. Furthermore, the limits of variations thus obtained are normally so great that it is difficult to define them for pathological comparison.

The author is indebted to Dr. Edward Quintard, director, and to Dr. A. F. Chace and other members of the medical department, for the opportunity to study the cases reported in this paper. He also wishes to express his appreciation to Prof. V. C. Myers, of this laboratory, for suggestions and aid in the preparation of the manuscript.

[20] Jour. Biol. Chem., 1916, xxiv, 203.

[21] Data taken from Table I.

[22] Data taken from Table III.

[23] Data recalculated from Tables I and II.

[24] This is in harmony with the more recent conclusions of Jonas L., and Austin, J. H.: AM. JOUR. MED. SC., 1916, cli, 560.

A CLINICAL STUDY OF CHLORIDE EXCRETORY FUNCTION.

By C. C. Wolferth, M.D.,
PHILADELPHIA.

(From the William Pepper Laboratory of Clinical Medicine and the Henrietta Heckscher Fellowship in Medical Research, School of Medicine, University of Pennsylvania.)

Introduction. The purpose of this investigation has been to study the value, as a clinical test, of the method of measuring sodium chloride excretory function, recently introduced by McLean.[1]

McLean has modified the formula devised by Ambard and Weill[2] to express the laws of excretion of sodium chloride in normal individuals, so that, given the data of rate of excretion of urine, concentration of chloride in the urine and the body weight of the subject, the concentration of chloride which would be found in the blood plasma could be calculated, provided the excretory function was normal. This modified formula is expressed as follows:

$$\text{Plasma chloride} = 5.62 + \sqrt{\frac{\text{Gm. NaCl per day} \sqrt{\text{Gm. NaCl per liter}}}{4.23 \times \text{body weight in kilos.}}}$$

The figure 5.62 refers to the normal threshold for chlorides, or concentration in the plasma at which excretion begins. Ambard and Weill found that excretion began when the concentration of chlorides in the blood plasma had risen above 5.62 per liter. The figure 4.23 is a constant introduced into the formula.

The theoretical concentration of plasma chloride calculated from the formula may then be compared with the actual concentration found by analysis of the blood plasma. The supposed threshold of beginning excretion for any case under study may be calculated from the following formula:

$$\text{Threshold} = \text{plasma chloride} - \sqrt{\frac{\text{Gm. NaCl per day} \sqrt{\text{Gm. NaCl per liter}}}{4.23 \times \text{body weight in kilos.}}}$$

McLean found in a large series of examinations in normal individuals that the theoretical concentration corresponded fairly closely with the concentration actually found. He then applied the method to the study of pathological conditions[3] and found that relatively increased concentration of chlorides in the plasma occurs especially in certain forms of cardiac and renal disease; that edema

[1] Jour. Exper. Med., 1915, xxii, 234.
[2] Semaine méd., 1912, xxxii, 217.
[3] McLean, F. C.: Jour. Exper. Med., 1915, xxxii, 366.

is usually accompanied by a relatively increased concentration of chlorides in the plasma, also that chloride and urea functions may be quite independent of one another.

The method of studying chloride excretory function hitherto most generally employed has been the test of the ability of the kidneys to excrete salt added to the diet. The patient is put upon a constant daily chloride intake until equilibrium between intake and excretion is established. Then on a certain day, 10 grams additional sodium chloride are given. If less than 85 per cent. of the added chloride is excreted within forty-eight hours it is interpreted as a retention.

Frothingham[4] studied 40 cases of chronic nephritis, comparing the test of ability of the kidney to excrete added salt with certain other diagnostic and prognostic tests of renal disease. Of the 40 cases, but one showed no impairment of ability to excrete added salt, whereas 14 excreted phthalein in normal amount. Frothingham's table shows that 9 of the cases with normal phthalein had very markedly impaired ability to excrete the added chlorides. Frothingham concluded that the added salt test is the best functional test for the detection of early chronic nephritis, but that it is of not much value in prognosis, since the ability to excrete added chloride may be greatly impaired relatively early in the course of the disease.

O'Hare[5] has studied 15 cases of nephritis by McLean's method of testing chloride excretory function and compared the results with those obtained by the Hedinger and Schlayer two-hour renal test and test of ability to excrete added chloride. He concludes that the McLean test is more satisfactory than the others.

Although the added salt test is undoubtedly of great value in the study of nephritis, it has many obvious disadvantages. The patient should be in a hospital, preferably under the care of a nurse trained specially to give metabolic diets. The test requires five or six days' time to be carried out properly. During this time all the urine must be carefully saved. If, as not infrequently occurs in nephritic cases, the patient vomits after the administration of the added salt the test is lost. Thus its application must be limited almost entirely to the comparatively small proportion of cases that can be studied in hospitals. On the other hand the method of studying excretion of chloride devised by McLean is relatively easy to carry out. It is not dependent upon any diet. It requires but two analyses. It does not necessitate having the patient in a hospital subject to the expense and loss of time incident to the added salt test. Therefore, if by the McLean test equally satisfactory information as to renal adequacy for chloride excretion could be obtained, it would be well worth adopting as a clinical test. For this reason we have tried the method in a series of cases, which have received careful

[4] Am. Jour. Med. Sc., 1915, cxlix, 808.
[5] Arch. Int. Med., 1916, xvii, 711.

clinical study and whose renal function has been tested by other methods.

METHODS. The technic of collecting specimens was carried out as recommended by McLean. The procedure was instituted usually three to four hours after the last meal. The patient was given 180 c.c. of water to drink. Thirty minutes later a seventy-two minute collection of urine was begun. In the middle of this period, blood was withdrawn and immediately shaken with a few crystals of potassium oxalate to prevent clotting. If the patient was unable to void exactly at the end of the seventy-two minute period, the period during which the urine was collected was noted to the nearest minute. The urine was measured to the nearest cubic centimeter. The blood was centrifuged for twenty minutes at high speed. The plasma was drawn off by pipette and analyzed for chloride content according to the method of McLean and Van Slyke.[6] The standard solutions were tested frequently to ensure their accuracy. Two c.c. portions of plasma were used. Nearly all the tests were made in duplicate. The urinary chlorides were determined by a modified Volhard method.

During the course of the work my attention was called by Dr. J. Harold Austin to the variability in the carbon dioxide binding capacity of plasma when no precautions have been taken to prevent escape of carbon dioxide from the whole blood. Gürber,[7] Petry[8] and others have noted that if the carbon dioxide tension of the serum were increased the cells became richer in chloride. If carbon dioxide is permitted to escape from the whole blood the plasma becomes more alkaline, so that in the mechanism of reëstablishing equilibrium of acids and bases between plasma and cells the chloride goes over from cells to plasma probably in the form of hydrochloride acid. Consequently when no attempt has been made to prevent the escape of carbon dioxide from the whole blood the chloride content of the plasma is found 0.200 to 0.500 grams per liter higher than when this loss of carbon dioxide has been prevented. The amount of migration of chloride from cells to plasma is directly dependent upon the amount of escape of carbon dioxide from the whole blood. Thus while the method of taking blood, which was recommended by McLean, is permissible for clinical determination in which small variation in threshold is not to be regarded as of great significance, a source of error is excluded by preventing the escape of carbon dioxide from the whole blood. To prevent this escape of carbon dioxide, and consequently the variable amount of migration of chloride from cells to plasma, the method of withdrawing blood under albolene, recommended by Van Slyke[9] for determination of

[6] Jour. Biol. Chem., 1915, xxi, 361.
[7] Sitzungsb. d. phys-med. Gesellsch. zu Würzburg, 1895, 28–37.
[8] Hofmeister's Beitrage, 1902, iii, 260.
[9] Personal communication to Dr. J. H. Austin.

carbon dioxide combining power of the plasma, was used in the latter part of the work. Taking this precaution the normal plasma chloride threshold is found to be approximately 5.30 grams per liter instead of 5.62 grams per liter.

I. *Non-nephritic Group without Chloride Accumulation.* In Table I is presented a group of 10 cases supposedly without nephritis or any circulatory disturbance in the kidneys. In this group the difference between the actual and theoretical concentration of plasma chloride has varied between −0.18 and +0.12 grams per liter. McLean, in a series of seventy-two observations, found slightly greater variations.

TABLE I.—NON-NEPHRITIC GROUP WITHOUT CHLORIDE ACCUMULATION.

Case.	Age.	Sex.	Diagnosis.	Sodium chloride, grams per liter.			
				Actual.	Calculated.	Difference.	Threshold.
I	46	M.	Angina pectoris	5.87	5.88	−0.01	5.61
II	29	M.	Endothelioma of lymph nodes	5.90	5.96	−0.06	5.56
III	25	M.	Traumatic epilepsy	6.17	6.26	−0.09	5.53
IV	23	M.	Luetic aortitis	5.87	5.83	+0.04	5.66
V	63	M.	Tumor of pons	5.63[10]	5.57[10]	+0.06	5.36[10]
VI	30	M.	Gastric neurosis	5.97	6.05	−0.08	5.54
VII	26	M.	Streptococcic bacteremia	5.81	5.96	−0.15	5.47
VIII	57	M.	Chronic myocardial disease; arteriosclerosis	5.81	5.88	−0.07	5.55
IX	16	F.	Bronchial asthma	5.56	5.72	−0.18	5.44
X	57	M.	Arteriosclerosis	5.59[10]	5.47[10]	+0.12	5.42[10]

II. *Non-nephritic Group with Chloride Accumulation.* In Table II are included 8 cases which show elevated chloride threshold, although they were considered after careful study in the hospital to be non-nephritic.

Cases XI and XII.—Entered the hospital with edema, due to cardiac decompensation. On admission both showed high threshold for chlorides. After the edema had subsided the threshold returned to normal.

Case XIII.—The chloride studies were made in this case of luetic cirrhosis of the liver, during a period when the patient had marked ascites, bilateral hydrothorax, and edema of the legs. At that time the phthalein excretion was 20 per cent. in two hours. The urine contained a cloud of albumin. Later when the collections of fluid has disappeared the phthalein rose to 60 per cent.; the urine showed only a faint trace of albumin. The retention of chlorides was probably due to circulatory disturbances in the kidneys.

Case XIV.—Diagnosis: cardiac decompensation, secondary cirrhosis of the liver. When the chloride study was made the patient's abdomen was steadily filling with fluid. There was almost complete anuria. After withdrawal of most of the fluid a fair urinary excretion was established. Tests made at this time showed the chloride threshold very much lower.

[10] Blood taken under albolene.

Case XV.—This case apparently belongs to the type described by Christian[11] as having disturbed salt elimination, but not, strictly speaking, actual nephritis. This man gave a history of always having eaten large amounts of salt. To test his statement a twenty-four hour specimen of urine examined for sodium chloride content while he was on the ordinary ward diet showed 29 grams. The chloride threshold was markedly above the normal on two examinations. During this time he had slight edema. He was then placed on a fixed low chloride intake and weighed every day at exactly the same time. On the day 10 grams sodium chloride was added to the diet he weighed 1.5 kilos more than on the preceding day. On that day none of the added chloride was excreted. On the following day, however, 7.9 grams extra chloride was excreted. This man has continued under observation for five months on a somewhat limited salt intake. He has shown no further tendency to edema.

Case XVI.—This case was diagnosed as probable early renal tuberculosis. The urine never showed more than a trace of albumin. The phthalein excretion was 35 per cent. in two hours. Two c.c. indigo-carmine were injected intravenously and the ureteral orifices observed for evidence of excretion. At the end of eight minutes a faint blue stream was seen coming from the left ureter. The amount was not materially increased at the end of twenty minutes. No excretion was observed from the right ureter in twenty minutes. Therefore, whatever may have been the primary disease the case had actual renal inadequacy when these studies were made. The elevated threshold for chlorides may be considered as one of the expressions of this inadequacy.

Case XVII.—The elevated chloride threshold in this case is difficult to explain. The urine examination, blood-pressure readings, phthalein tests, and blood urea analysis gave no evidences of nephritis. The patient was voiding only from 400 c.c. to 660 c.c. urine for several days before the first test of chloride excretory function was made. He was then given theocin, 0.2 gram three times a day for three days and the studies repeated. The plasma chloride, meanwhile, had dropped 0.5 milligram per cubic centimeter. However, the chloride threshold was still elevated above the normal.

Case XVIII.—This case also gave no evidences of renal inadequacy. The diagnosis made was chronic myocardial disease with anginoid attacks. The statement was made by the patient's physician that there had been edema of the legs before admission to the hospital. None, however, was observed during his stay in the ward. No material change in the threshold was observed after giving theocin, 0.2 gram, three times a day for three days or after tincture of digitalis, 0.65 c.c., three times a day for five days. The only suggestive finding in this case was the fact, that the urinary concentration of chloride was always low.

[11] Christian, H. A.: Am. Jour. Med. Sc., 1916, cli, 630.

TABLE II.—CASES PRESUMABLY NON-NEPHRITIC WITH CHLORIDE ACCUMULATION.

Case.	Age.	Sex.	Date.	Diagnosis.	Edema.	Sodium chloride, grams per liter of plasma.			
						Actual.	Calculated.	Difference.	Threshold.
XI	63	M.	Oct. 26	Cardiac decompensation	+	6.25	5.86	+0.39	6.01
			Nov. 16		0	6.00	5.92	+0.08	5.70
XII	36	M.	Nov. 2	Cardiac decompensation	+	6.69	5.88	+0.81	6.43
			4		+	6.69	5.95	+0.74	6.36
			16		0	6.43	6.29	+0.14	5.76
XIII	42	M.	Nov. 21	Luetic cirrhosis	+	6.34	5.84	+0.50	6.12
XIV	67	F.	Jan. 7	Cardiac decompensation; secondary cirrhosis	+	6.65	5.68	+0.97	6.59
			Mar. 24		+	6.31	5.88	+0.43	6.05
XV	26	M.	Dec. 20	Bronchial asthma	+	6.62	6.19	+0.43	6.05
			23			6.50	5.99	+0.51	6.13
XVI	28	F.	Feb. 22	Renal tuberculosis (?)	0	6.12[12]	5.63[12]	+0.49	5.79[12]
XVII	50	M.	Nov. 8	Sciatica	0	6.81	5.95	+0.86	6.48
			18			6.31[13]	5.84	+0.47	6.09
XVIII	63	M.	Nov. 8	Myocardial weakness	+	6.37	5.84	+0.53	6.15
			18			6.31[13]	5.77	+0.54	6.16

III. *Chloride Excretory Function in Nephritis.* In Table III are presented the results of study in 22 cases of nephritis, arranged according to the clinical classification employed in the University Hospital.

Advanced Glomerulonephritis: Of 11 cases studied, 9 showed high chloride threshold. Of this group 3 cases (XX, XXIV, and XXVI) showed no lowering of chloride threshold under the influence of vapor baths and salt-free diet.

CASE XIX, whose threshold was high when the first studies were made after nineteen days' treatment with salt-free diet and vapor baths, showed a drop of 0.78 gram chloride per liter of plasma. Two days after the administration of 10 grams of sodium chloride, a slight amount of which was vomited, the threshold had again risen slightly beyond its original point. Case XXVIII, in addition to advanced nephritis, on admission had slight cardiac decompensation with edema of the legs. Under rest and digitalis the edema rapidly disappeared, but a hematuria which had been quite marked on admission, persisted. The patient was then put upon salt and protein-low diet and given a hot pack every other day. The hematuria gradually diminished until there were no macroscopic evidences of blood in the urine. Erythrocytes could still be found under the microscope, however. A McLean test at this time showed that the threshold was not raised above the normal limit. As a check upon this finding the test of ability to excrete 10 grains additional sodium chloride was made. But 4.9 grams were excreted in forty-eight hours. The urine which had been clear for about two weeks previously, on the day chloride was administered, became quite hemorrhagic in appearance. The red color gradually disappeared in the course of a week.

[12] Blood withdrawn under albolene.
[13] Had received theocin for three days.

CASES XIX and XXVIII. These cases illustrate the point that the finding of a normal chloride threshold must not be regarded as conclusive evidence that the kidney function for chloride excretion is normal. In Case XXVIII the sudden return of hematuria after the administration of sodium chloride suggests very strongly that the salt acted as a renal irritant.

CASE XXIX.—This patient, who had the greatest waste nitrogen retention of any case in the group, showed no accumulation of chloride in the plasma. A test of ability to excrete added chloride could not be carried out as the patient was bordering on uremia. In this case the diagnosis of advanced glomerulonephritis was confirmed by autopsy a few weeks after the patient had left the hospital.

Thus of 11 cases of diagnosed clinically as advanced glomerulonephritis, 9 showed impairment of renal chloride excretory function by having a high chloride threshold, a tenth showed no elevation of the threshold, but impairment of ability to excrete added sodium chloride, while the eleventh, one of the most severe cases in the group, showed a normal plasma chloride, but could not be studied as to his ability to excrete added chloride.

Intermediate Glomerulonephritis. In this group of 4 cases 2 showed a high threshold for chlorides.

CASE XXXI.—This case is of interest because the plasma chloride threshold was high, whereas the ability to excrete added salt was practically unimpaired. On admission to the hospital this patient had advanced neuroretinitis with many hemorrhages. The blood-pressure was 200 systolic and 110 diastolic. The urine showed a faint trace of albumin with only an occasional cast. The specific gravity tended between 1.005 and 1.009, but on a dry diet rose to to 1.028. The blood nitrogen was 28 milligram per 100 c.c. The phthalein excretion was 55 per cent. in two hours. The plasma chloride threshold at this time was 6.44 grams per liter. Of 10 grams added salt, 7.9 grams were excreted in forty-eight hours. The patient was kept quietly in bed on a salt-free low protein diet. The retinitis improved slowly. The blood-pressure fell to 145 systolic and 88 diastolic. Headache, which had been a troublesome feature of the case, disappeared. The improvement has continued over a period of six months, during which time the patient has been on a restricted salt intake.

Early Glomerulonephritis. One case, diagnosed early glomerulonephritis, was studied, as follows:

CASE XXXIV.—This patient came to the hospital, to the service of Dr. de Schweinitz, complaining of dimness of vision. He was found to have a peculiar form of proliferative retinitis, apparently not of renal origin. Physical examination was entirely negative, except for slight enlargement of the heart to the left, accentuated aortic second sound, and slight sclerosis of the peripheral arteries. The blood-pressure was only slightly elevated.

TABLE III—GROUP OF NEPHRITIC CASES

TABLE III.—GROUP OF NEPHRITIC CASES.

Case.	Age.	Sex.	Date.	Sodium chloride, grams per liter.				Urine.			Blood-pressure.		Phthalein per cent.	Non-protein blood, mgr. in 100 c.c.	Blood urea, mgr. in 100 c.c.	Eye-ground examination.
				Actual.	Calculated.	Difference.	Threshold.	Albumin.	Casts.	Specific gravity.	Systolic.	Diastolic.				
ADVANCED GLOMERULONEPHRITIS.																
XIX	39	F.	Apr. 17	6.03[16]	5.50[16]	+0.53	5.83[16]	Cloud	Few	1.008–1.011	200	140	1		192	Renal retinitis.
			27	5.69[16]												
			Mar. 6	5.25[16]	...	...	...									
			Mar. 26	6.03[16]	5.32[16]	−0.71	6.01[16]	....	..	....	250	160				
XX	44	M.	Feb. 25	6.25[16]	5.42[16]	+0.83	6.13[16]	Cloud	Many	1.010–1.012	210	135	Trace	.....	142	Angiosclerosis.
			Mar. 4	6.22[16]	5.47[16]	+0.75	6.05[16]	....	..	....	178	120	7			
			8	6.22[16]	5.53[16]	+0.69	5.99[16]									
XXI	40	F.	Dec. 4	6.81	5.90	+0.91	6.53	Cloud	Many	1.009–1.010	204	138	Trace	.....	229	
XXII	47	F.	Dec. 18	6.47	5.75	+0.72	6.34	Cloud	Many	1.012–1.015	262	141	15	.....	83	Neuroretinitis.
XXIII	39	M.	Oct. 26	6.62	5.70	+0.92	6.54	Cloud	Many	1.009–1.013	186	115	Trace	76	....	Angiosclerosis.
			Nov. 1	6.19	5.64	+0.55	6.17	....	..	....	135	97				
XXIV	53	M.	Nov. 30	6.00	5.73	+0.27	5.89	Trace	Many	1.010–1.012	225	165	12	.....	96	Neuroretinitis.
			Dec. 4	6.02	5.65	+0.37	5.99									
			17	6.22	5.81	+0.41	6.03	....	..	....	....	....	15	.....	115	
XXV	35	M.	Nov. 29	6.47	5.87	+0.60	6.22	Trace	Occas.	1.019–1.027	190	102	25	56	....	Disk, margins blurred; one hemorrhage.
			Dec. 3	6.37	5.81	+0.56	6.18									
XXVI	24	M.	Nov. 4	6.12	5.71	+0.41	6.03	Heavy	Many	1.010–1.025	242	180	33	46	....	Wide-spread retinitis.
			15	6.12	5.82	+0.30	5.92	....	..	....	178	135	37			
			29	6.25	5.81	+0.44	6.06	Cloud								
			Dec. 3	6.28	5.74	+0.54	6.16									
XXVII	45	M.	Feb. 8	6.09	5.69	+0.40	6.02	Light cloud	Few	1.015–1.019	185	135	35	.....	39	Hemorrhages; neuroretinitis
XXVIII	34	M.	Mar. 21	5.53[16]	5.43	+0.12	5.42	Light cloud	Very few	1.005–1.014	182	78	12	.....	80	Negative.
XXIX	34	M.	Mar. 27	5.48[16]	...	...	...	Cloud	Many	1.009–1.014	138	49	20			
			29	5.56[16]							175	110	Trace	.....	417	Negative.
INTERMEDIATE GLOMERULONEPHRITIS.																
XXX	24	M.	Feb. 1	6.41	5.99	+0.42	6.04	Cloud	Many	1.013–1.015	160	120	30	...	90	
XXXI	48	F.	Dec. 21	6.56	5.74	+0.82	6.44	Trace	Few	1.005–1.020	200–145	110–88	55–68	28	....	Neuroretinitis.
XXXII	24	F.	Feb. 16	5.62[16]	5.54[16]	+0.08	5.38[16]	Faint trace	None	1.010–1.012	190	135	35	.....	31	Angiosclerosis.
XXXIII	39	M.	Mar. 9	5.66[16]	5.55[16]	+0.11	5.41[16]	Cloud	Many	1.012–1.025	176	110	55	.....	37	Angiosclerosis
EARLY GLOMERULONEPHRITIS.																
XXXIV	39	M.	May 27	5.75[16]	5.46[16]	+0.29	5.59[16]	None	None	1.021	155	102	56	.....	25	Proliferative retinitis.
CHRONIC DEGENERATIVE NEPHRITIS.																
XXXVI	29	F.	Apr. 17	6.25[16]	5.62[16]	+0.63	5.93[16]	Boils solid	Many	1.023	150	110	35	.....	36	Negative.
			19	6.12[16]	...	...	...	....	..	....	135	90				
			May 4	6.03[16]												
XXXVII	34	M.	Jan. 22	6.37	5.96	+0.41	6.03	Cloud	Many	1.028	....	....	60	.....	60	Old hemorrhages.
XXXVIII	56	M.	June 4	6.40[16]	5.33[16]	+1.07	6.37[16]	9 gm. per liter	Many	1.015	160	90	Trace	.....	261	Slight angiosclerosis.
RENAL SCLEROSIS.																
XXXIX	55	M.	Nov. 27	6.12	6.02	+0.10	5.72	Faint trace	Few	1.031	....	....	52	.....	48	Negative.
XL	63	F.	Mar. 11	5.78[16]	5.66[16]	+0.12	5.42[16]	Cloud	Many	1.009–1.035	250	130	35	.....	....	Angiosclerosis.
ACUTE PYELONEPHRITIS.																
XLI	37	F.	Nov. 8	5.62	5.51	−0.11	5.51	Cloud	None	1.010–1.015	110	65	10 Trace	187	442	

[16] Blood taken under albolene.

Numerous urine examinations failed to show either albumin or casts. The phthalein excretion was normal. There was no accumulation of urea in the blood. The sodium chloride threshold was only slightly elevated. The ability to excrete added sodium chloride was markedly diminished, but 2 out of 10 grams added salt being excreted in forty-eight hours. The degree of impairment of renal function for chlorides revealed by the inability to excrete added chlorides would scarcely have been suspected from the very slight elevation of the threshold.

Chronic Degenerative Nephritis. But 3 cases diagnosed as chronic degenerative nephritis were studied. All showed a high threshold. The chloride excretion seemed more disturbed than the phthalein or urea excretion, except in Case XXXVIII, in whom almost all kidney function had ceased.

Renal Sclerosis. The 2 cases diagnosed renal sclerosis studied, showed no retention of chloride.

Acute Pyelonephritis.

CASE XLI.—This was a case of acute pyelonephritis; the urine contained a large amount of pus and gave pure culture of Bacillus mucosus capsulatus. It is of interest chiefly because of the low chloride threshold in contrast to a tremendous retention of urea and a phthalein excretion varying from 10 per cent. to a trace. The diagnosis of acute pyelonephritis was confirmed by autopsy.

Poisoning by Mercuric Chloride.

TABLE IV.—POISONING BY MERCURIC CHLORIDE.[15]

Case.	Days after taking mercuric chl.	Sodium chloride, grams per liter.				Urine.		Phthalein percentage.	Remarks.
		Actual.	Calculated.	Difference.	Threshold.	Albumin.	Casts.		
XLIII	1	4.56	5.30	−0.74	4.56	Cloud	Many	10	Modified
	2	4.62	5.30	−0.68	4.62	"	"	25	Lambert
	4	4.92	5.30	−0.38	4.92	"	"	65	treatment.
	9	5.50	5.31	+0.19	5.49	Light cloud	None	43	8th day
	14	5.81	5.40	+0.41	5.71	Faint trace	Occasional	48	Lambert treat. dis.
XLIV	1	5.25	5.44	−0.19	5.11	Trace	"	7	Lambert
	4	5.27	5.36	−0.09	5.21	"	None	50	treatment
	9	5.87	5.46	+0.41	5.71	"	"	55	dis. 5th day.

CASE XLIII (Table IV).—White, male, age twenty-one years, weight 60 kilos. Took 0.5 gram mercuric chloride, thinking it was a headache remedy. Fifteen minutes later he discovered his mistake, took seven eggs, some starch, and milk. Brought immediately to the hospital, where a modified Lambert treatment was instituted within an hour of the time he had taken the mercuric chloride. During the first twenty-four hours he voided over 4000 c.c. of urine. For several days the urine showed enormous numbers of casts and renal epithelium and a cloud of albumin. The phthalein, which had been low, returned to normal until the Lambert treatment was

[15] All blood taken under albolene.

discontinued, when it dropped slightly again. The blood urea never rose above 0.43 gram per liter.

The concentration of chlorides in the plasma after twenty-four hours of the Lambert treatment dropped to 4.56 grams per liter the lowest figure that has been found in the laboratory. The urine at the time showed only a faint trace of chlorides, not sufficient to determine quantitatively by the McLean and Van Slyke method for chlorides. Three days later there was a slight rise in concentration of chlorides in the plasma, but still only a trace of chloride in the urine. After the Lambert treatment was discontinued and a diet containing more salt given the plasma chloride rose rapidly until there was evidence of distinct retention.

Case XLIV (Table IV).—White, male, aged twenty-four years, weight 69 kilos. While intoxicated he took 0.5 gram mercuric chloride dissolved in 150 c.c. of water. Vomited about three hours later. Then came to the hospital, where a modified Lambert treatment was instituted immediately. There was good diuresis, 3200 c.c. of urine passed in the first twenty-four-hour period. The phthalein was 7 per cent. at the first examination, but subsequently rose to normal. The urine never showed more than a trace of albumin and a few hyaline and granular casts. Highest blood urea figure 0.300 gram per liter.

The behavior of the chloride in the case resembled that of Case I. During the Lambert treatment the concentration in plasma was below the normal threshold. After the Lambert treatment was stopped there was distinct retention of the chlorides.

These cases of mercurial poisoning show how a concentration of chloride in the plasma below a normal threshold may be reached by vigorous measures of elimination. In both cases at the time the urine examinations and phthalein excretion showed most damage to the kidney the plasma chloride concentration was well below the normal threshold. Later, when the evidences of nephritis had subsided, the Lambert treatment discontinued and the patient allowed to take a diet containing salt, the concentration of chloride in the plasma quickly rose to a point where it was quite evident that there was distinct retention.

Eclampsia. Through the kindness of Dr. B. C. Hirst it was possible to study the plasma chloride in 5 cases of eclampsia and 2 cases bordering on eclampsia. Unfortunately in 2 of the cases the condition of the patient was such that accurate studies of urinary excretion could not be carried out.

The 5 cases of eclampsia all show a high plasma chloride concentration. Three in whom urinary studies could be carried out showed marked elevation of chloride threshold. In Case XLV (Table V), studied while rapid improvement was taking place, the plasma chloride fell 0.22 milligram per cubic centimeter in twenty-four hours. The two preëclamptics also showed chloride retention;

in 1 case, quite marked; in the other, which was probably a combination of preëxisting nephritis and threatened eclampsia, not so marked. This chloride retention is in contrast to the very slight tendency for waste nitrogen to be retained in eclampsia.

TABLE V.—ECLAMPSIA.

Case.	Date.	Blood-pressure.		Blood urea. Mgm. per 100 c.c.	Sodium chloride, grams per liter of plasma.			
		Systolic.	Diastolic.		Actual.	Calculated.	Difference.	Threshold.
XLV	Mar. 29	205	135	30	6.00[16] 5.78[16]			
XLVI	Feb. 28				6.37	5.71	+0.66	6.28
XLVII	Feb. 26	138	105		5.76[16]	5.36[16]	+0.40	5.70[16]
XLVIII	Feb. 3			46	6.53			
XLIX	Dec. 30	220	196	26	6.62	5.94	+0.68	6.30
				Threatened Eclampsia.				
L	May 14	180	130	44	6.00[16]	5.32[16]	+0.68	5.98[16]
LI	May 14	220	145	64	5.69[16]	5.33[16]	+0.36	5.66[16]

Discussion. While the McLean method of studying renal chloride excretory function seems to give valuable information in many cases of nephritis, the results in each particular case must be regarded critically. Two cases of advanced nephritis in this series had marked impairment of their ability to excrete salt, yet the threshold at various times was found normal. On the other hand 2 cases with a very high threshold were able to sweep out added salt very efficiently. While a normal threshold does not necessarily signify that renal function for chlorides is unimpaired, a high threshold probably nearly always means impaired chloride excretion, whether this be due to actual renal disease or circulatory deficiency.

The marked effect produced by conditions interfering with the circulation in the kidney, such as passive congestion, must always be borne in mind. The threshold may be quite as high in cases of cardiac decompensation with edema as in the severest cases of advanced nephritis. The excretion of chloride is apparently far more influenced by passive congestion than is the excretion of urea.

The results of the work here presented agree in a general way with the conclusion of McLean that the chloride and urea functions may be quite independent of one another. Retention of chloride without retention of urea occurs very much more frequently than the reverse. But 2 cases were found in the series, in which there was a high blood urea figure and normal chloride threshold. Since both these cases were very ill, so that no other tests of renal adequacy for chlorides could be carried out, it is doubtful whether these cases really had good renal function for chlorides.

Summary. A study of the method of investigating renal excretory function devised by McLean has been made in a series of normal and pathological cases.

[16] Blood taken under albolene.

The application of Van Slyke's method of withdrawing blood to prevent escape of carbon dioxide and the effect of this procedure upon the chloride content of the plasma were discussed.

A group of individuals with presumably normal renal function was found to conform fairly closely, in the excretion of chlorides, to the laws of excretion formulated by Ambard and Weill.

A group of cases diagnosed as non-nephritic showed elevated threshold for chlorides. Most of these cases showed evidences of circulatory disturbances in the kidneys.

Studies of chloride excretory function were made in 21 cases of nephritis, 7 cases of eclampsia and threatened eclampsia, and 2 cases of mercuric chloride poisoning.

CONCLUSIONS. 1. An elevated plasma chloride threshold, when circulatory disturbances can be excluded, is valuable evidence of the presence of nephritis.

2. A normal threshold may be found in cases with marked impairment of ability to excrete chlorides, particularly if the patient has been kept on a regime including salt-free diet and measures to stimulate elimination.

3. Sodium chloride added to the diet is sometimes excreted as completely by impaired kidneys working under the stimulation of a high chloride content of the plasma as by normal kidneys working under normal threshold; added chloride may be retained when the threshold is normal. Therefore the information gained by both methods of study is desirable,.

4. Chloride excretory function is impaired in nearly all cases of nephritis.

5. Chloride excretory function is much more disturbed in eclampsia then is urea excretory function.

FAMILIAL EPISTAXIS; A CASE REPORT.[1]

BY HENRY B. RICHARDSON, M.D.,
BOSTON.

OSLER, in 1901[2] described a "family form of recurring epistaxis, associated with multiple telangiectases of the skin and mucous membranes." Since then he has collected from the literature and from his own experience, data on eight families afflicted with the disease.[3] Hutchinson and Oliver[4] recently reported a remarkable family, in which it occurred in three successive generations. Osler's description well sums up the disease. Its hereditary nature is particularly striking. Neither sex predominates. The attacks of

[1] From the Medical Clinic of the Peter Bent Brigham Hospital.
[2] Johns Hopkins Hosp. Bull., 1901, xii, 333. [3] Ibid., 1907, xviii, 402.
[4] Quart. Jour. of Med., 1916, ix, 67.

epistaxis may begin in early life, and recur frequently even to advanced age, and are associated with bleeding of the mucous membranes of the mouth, sometimes of the skin as a result of trauma, and possibly of the gastro-intestinal tract and lungs. The telangiectases, though occurring chiefly in the mucous membranes of the mouth and nose, may appear over the body surface in general, particularly on the trunk and hands. The anemia produced is of a pronounced secondary type. The blood coagulation time is normal. In these several papers[5] the literature of the subject is given in sufficient detail to warrant its not being discussed again.

Case I.—C. S. was admitted to the medical wards of the Peter Bent Brigham Hospital on January 28, 1916. He is a German, born in Germany, aged fifty-three years, and has lived in this country for twenty-eight years. The father died of apoplexy when the patient was four years old. The mother suffered from epistaxis, though never to such an extent as the patient. She died of an operation during childbirth. Of the four other children, two boys died in infancy, at the ages of six and eighteen months. A brother and sister were still living and well when last heard from, though the latter also was subject to bleeding from the nose, less severe than that of the patient. Each of these had a daughter, of whom nothing is known as to epistaxis or spots. A maternal cousin was known to have spots on her face, and to be subject to epistaxis, and her two sons and two daughters were all subject to epistaxis. Further details of the family's history are unfortunately missing, as no response was received to letters of inquiry sent to Germany.

The patient married twice. Of the two sons by the first marriage in 1888, the elder is free from symptoms, but the younger, recently married, is subject to epistaxis (Case II). The patient's first wife died four years ago. In 1913 he married again, and has one child, a year old, who so far has had no nosebleeds. The patient is a teamster on an express wagon, working eight or nine hours a day, and doing much heavy lifting. He is accustomed to taking one or two bottles of beer daily, a cup of tea and a cup of coffee, but rarely smokes. He has had no illnesses, except an occasional mild sore throat, and a history of "kidney trouble," four years previous, for which he was treated by a private physician. He denies having had venereal disease.

Symptoms of the present illness began at least ten years ago, when spots were noticed on his face. These have been constantly present though varying in number, and have showed a tendency to bleed slightly if scratched. About four years previous to his admission he became subject to exhaustion, dizziness, pallor, and yellowness of the skin. This condition increased in severity. The attending physician is said to have noticed that the sclerae were yellow. The

[5] Osler: Quart. Jour. of Med., 1907–08, i, 53; Parkes Weber, Lancet, London, 1907, ii, 160.

patient then began to have left temporal headache, relieved by spontaneous discharge from the ear. Nevertheless, he continued weak for three or four months, and his weight dropped from 150 to 135 pounds. His health then improved and remained good until about a year ago, when he first had a hemorrhage from the nose, "als ob ein Vieh geschlactet werde," which he estimated at about one quart in amount, followed by marked weakness, pallor, and vertigo. After six or seven weeks he again recovered and felt well and strong, with the exception of a left lateral headache, until nine days before admission. Then he had another profuse nasal hemorrhage, estimated this time at about one pint, and became weak and pale. Bleeding recurred each time that he blew his nose, but was not so severe. Shortly after the hemorrhage he noticed tarry stools. Both of his severe hemorrhages have occurred in winter, and he has noticed a tendency to bleed on the colder days of all seasons. He has never bled abnormally from cuts. He entered the hospital without further change in condition.

The physical examination showed him to be a well-developed, powerfully muscled, and intelligent German, past middle age, and in no obvious discomfort. The face is pale and has an orange-yellow tinge. On it are numerous, irregularly distributed, cherry-red areas, averaging about 2 mm. in diameter, the border of many of which is formed by a close network of serpentine lines. On pressure the color disappears for an instant. These are most numerous in the region about the mouth and nostrils, particularly the cheeks, and on and just below the lower lip. (This facial distribution of telangiectases strikingly resembles that in one of Osler's patients, of whom a colored drawing is reproduced in Osler's paper in the *Quarterly Journal of Medicine*). There are many smaller areas above and close to the eyebrows. There is a moderate yellowish pigmentation of the palate, on which a few red patches similar to those on his face are visible, as well as two or three on the buccal mucous membranes. On the right side of the nasal septum, about 2 cm. from the nares, is an area 5 to 10 mm. long, bright cherry red in color, consisting of three elongated patches. Beside this is a white area, suggestive of scar tissue. On the left nasal cavity are several small blood clots, and on the septum there is a circle of red nodular elevations, with a shallow depression in the center. Rhinoscopy, by Doctor C. B. Walker, disclosed numerous lesions of this type on the septum and turbinates.

The trunk and lower extremities are clear, but on the dorsum of the right finger there is a red area about 1.5 mm. in diameter, with sharply defined borders which disappear on pressure. Under three of the nails are similar minute areas. On the glans penis are two more, but these cannot be pressed out. The left testicle is enlarged. Transillumination showed the enlargement to be a hydrocele. There are no herniæ, although the hernial rings are slightly enlarged.

Ophthalmoscopic examination failed to show hemorrhage or other abnormalities of the retinæ. Examination of the circulation was essentially negative, except for a slight enlargement of the heart to the left, a blowing systolic murmur best heard at the pulmonary area, and a moderately increased arterial pulsation. The blood-pressure was 80 systolic, 36 diastolic.

The blood showed a well-marked secondary anemia, the hemoglobin being 55 per cent., the erythrocytes 3,400,000. The white count was 9300. The smear showed 70 per cent. of neutrophiles, 10 per cent. of small mononuclears, 13 per cent. of large mononuclears, 3 per cent. of eosinophiles, 1 per cent. of basophiles, and 3 per cent. of transitional cells. The erythrocytes showed poikilocytosis and anisocytosis. The coagulation time as measured in a single glass tube was four minutes. The urine contained at first the slightest possible trace of albumin, then a large trace, but none on three subsequent examinations. Neither erythrocytes nor casts were found in the urine on any of five examinations. Gastric analysis demonstrated a hydrochloric acid deficit in each of three specimens, withdrawn at intervals of three-quarters of an hour after the Ewald test-meal by means of a Rehfuss tube. The Wassermann reaction, at first "plus minus," was later reported negative.

On the night of January 29, the patient lost a small amount of blood from the left nostril, and again on the following day, but not enough to soak a handkerchief. On January 31 the administration of saccharated ferrous carbonate 0.25 gram, three times daily, was begun. The patient continued to have slight hemorrhages from the left nostril up to two days before discharge. On February 7 the administration of calcium lactate, 1 gram four times daily, was begun, to be continued in the outdoor department. He was discharged on February 11, feeling better and stronger, but with no marked objective change, except an increase of 1,000,000 in the erythrocyte count. He visited the outdoor department at intervals and received prescriptions for iron and calcium lactate, the latter in decreased doses. He continued to have slight hemorrhages from the left nostril, and on one occasion small clots were found in the right. The hemoglobin gradually increased. On June 9 it was 72 per cent. (Sahli), and the erythrocytes numbered 4,800,000, an increase of 500,000 since discharge. The smear was normal, except for a marked achromia. The differential count showed normal relations as opposed to the low percentage of small mononuclears observed in the hospital. The leukocyte count was 5800, the blood-pressure 132 systolic and 81 diastolic, the urine entirely negative. The left border of the heart was normal and the systolic murmur had disappeared. There was no marked change in the telangiectases. The patient looked strong and healthy, and was again doing heavy physical work.

Case II.—R. S., aged twenty-five, younger son of the above, visited the outdoor department of the Peter Bent Brigham Hospital

on June 28, 1916, on request. He has been married for two years, having no children. His wife is in good health, but has had one recent miscarriage. He is a traveling salesman and undergoes no heavy exertion. His habits are excellent. He had measles in childhood, but has always been strong, except for a susceptibility to sore throats and colds. He has been able to play baseball and football at a preparatory school, and later on a university team. He denies having had any venereal disease.

Ever since he can remember he has had frequent epistaxis, averaging two or three times a week, and seven times during the last two weeks. The hemorrhages come from either nostril. Twice, an attack has consisted of a gush of blood, though usually they are less severe, and have always been readily controlled within two or three minutes by application of ice-water to the nose. They sometimes have come without obvious cause, but usually as a result of slight trauma or sneezing. He has often noticed that change of temperature, as in entering a hot boiler room, precipitates an attack. His wife has remarked on a blotchy appearance of his face, but he has never noticed spots there or elsewhere, except for a minute one on the upper arm. He has never bled freely from cuts.

A general physical examination shows an excellently developed man of good musculature, though slightly obese and flabby. The findings were negative except for the condition of the skin. On the left side of the nose, are two minute thread-like telangiectases of a radial arrangement. On the cheeks, under the melar bones, there is a slight telangiectatic enlargement of the finer vessels. This is also seen in the ears, especially in the fossa of the helix, and in both cases can be largely or entirely pressed out. On the end of the tongue is a round pink depressed area, about 1 or 2 mm. in diameter, and not affected by pressure. Rhinoscopy, by Dr. C. B. Walker, was negative, showing no telangiectases. On the skin by the right little finger nail is a minute cherry-red area, and similar ones under the third and fourth finger nails of the left hand. All these are blanched by pressure. There is a minute angioma on the right upper arm. No telangiectases are visible elsewhere.

The urine contains no sugar, albumin, erythrocytes, or casts. The blood-pressure is 122 systolic and 68 diastolic. The coagulation time as measured in a single glass tube is seven minutes. The hemoglobin by Sahli's method is 123 per cent. The erythrocytes number 6,700,000, the leukocytes 10,000. In the smear the erythrocytes are normal, as is also the differential count of the leukocytes. No abnormal types of cells are seen.

The interest in these cases lies mainly in their familial occurrence. As a symptom the epistaxis is very annoying to the individual and not infrequently serious owing to the severe secondary anemia that incapacitates. These families with hereditary multiple telangiectases associated with epistaxis are rare enough to justify this brief record of an additional family.

DIAGNOSIS OF EARLY PULMONARY TUBERCULOSIS.[1]

By James I. Johnston, M.D.,

PHYSICIAN TO THE MERCY HOSPITAL, PITTSBURGH, AND ASSISTANT PROFESSOR OF MEDICINE IN THE UNIVERSITY OF PITTSBURGH MEDICAL SCHOOL.

The recognition of early pulmonary tuberculosis belongs rather to the physician in general practice and to the internist than to those who devote their whole professional time to the care and management of tuberculous patients. Active tuberculosis is the only form that concerns the clinician, and is the only one of import to the patient. This fact, emphasized by Baldwin a few years ago, has not been fully appreciated by the profession. Early pulmonary tuberculosis, like the diagnosis of most chronic diseases in their early stages, cannot be made at one seance with the patient. Pulmonary tuberculosis which can be positively diagnosed at the first examination is one of established pathology and probable permanent damage. One must realize then at the outset that the diagnosis of this disease in its early stages, when amenable to cure, is very often a difficult problem, and its importance makes the time spent on solving this problem for a patient well worth while. When the problem is solved it is not only fair but absolutely essential to tell the patient whether or not the disease exists, because upon his coöperation depends the curability more than in any other disease. The chief complaint which these cases present is frequently suggestive of something remote from the seat of pathology. Epigastric pain, fatigue, loss of weight, palpitation, flushing, malaise, as well as the common ones of cough, fever, asthenia, or expectoration are among those offered by the patients. As in chronic diseases of the stomach and intestinal tract a study of the history of these cases is of prime importance. A definite knowledge of tuberculous association is of far more significance than that of diseased ancestry. An attack of pleurisy, especially if accompanied by effusion, is highly indicative of tuberculous potentiality. The identification of some local focus, either in the tonsil or cervical glands, is a possible indicator of the damaging infection in the lung.

An inquiry which elicits from the patient hemoptysis, even of the slightest degree, while not pathognomonic of tuberculosis, is a fairly accurate sign and deserves analysis. Again, analogous to the study of carcinoma, syphilis, and leukemias a history of great loss of weight without apparent cause to the patient, particularly with some or all of the foregoing factors, justifies suspicion of pulmonary tuberculosis. A brief record of the day's work and life and symptoms of such a patient during his waking hours deserves the utmost

[1] Read before the Westmoreland County Medical Society, Pennsylvania, April 4, 1916.

cognizance. The examination of the patient himself presents two aspects: (1) the physical, which up to the present time is still the more valuable, and (2) the laboratory, which is an important accessory and may in the future supersede the physical. The physical examination includes a prolonged study of recorded temperatures, weight studies under forced feeding, and repeated examination of thorax with recorded areas, the seat of rales. The laboratory examination comprises tests of the sputum, skin, blood, roentgen-ray findings, and the complement-fixation. In making observations of temperature study it is my own practice to supply the patient with an ordinary filing card, upon which definite hours are marked at which he is to take his temperature and record it. This is kept over a period of ten days, when he returns his card for my observation and analysis. At the same time he is placed on a mixture of milk, cream, and eggs, the equivalent of at least 1000 calories, which is added to his ordinary general diet. Also, his weight is noted before carrying out this plan and at its completion.

During this period of diagnostic study the patient is instructed to continue his ordinary occupation and in no way to modify his mode of living. The usual methods of physical diagnosis are carried out next to the naked thorax and a careful record made of suspected pathological findings. This is particularly true of voice transmission and the presence of rales. The so-called latent rale is diligently sought for and their location recorded and marked on a graphic figure.

At the second and subsequent examinations, should they be necessary, these locations and the presence of rales are carefully compared and checked up with former findings. Persistent slight rise in temperature, especially in the late afternoon, at the time of greatest fatigue, with increased pulse-rate, which should be observed at this time; no satisfactory gain in weight under the forced feeding; the presence of rales and particularly the latent rale in the same area formerly observed, spells presumptively early pulmonary suberculosis.

Sputum analysis, while always desirable, is really not a true factor in the early recognition of this disease, because its absence is not conclusive negative evidence and its presence usually denotes established tuberculous infection, with damage. The various skin tests, either the cutaneous or intracutaneous, as introduced by von Pirquet and others, have two values: (1) in the examination of children under eight to ten years of age, and (2) as a preliminary test to the subcutaneous tests as practised on adults. The eye test, or Calmette test, has fallen into disuse because of dangers to the eye; but some clinicians believe in its revival, as it has a greater prognostic interpretation than any of the others. Ordinary blood counts have comparatively little significance, although the presence of a slight leukocytosis of 10,000 to 12,000 is found in tuberculosis,

malaria, and carcinoma, and while differential counts show increased lymphocytosis, a condition which may also be present in syphilis. It was the hope of the roentgen-ray worker that by the fluoroscope and the plate early active tuberculosis could be readily solved. This has proved a chimera, because while the damaged lung is often apparent in its diseased parts on the plate, its activity can in no way be designated nor recognized. The fluoroscope, while showing the movement, is of little value in determining early pathological activity.

In this country the complement-fixation test for tuberculosis has best been presented by Craige, of the United States Army. This test in its technic is analogous to other complement-fixation tests, the most familiar of which is the Wassermann test for syphilis. This reaction is not only of value in suspected cases in which no physical signs are present, the best cases for cure, but also shows that cases which are considered in a state of cure are not entirely free from infection as long as this test is positive. The great value in this study along these lines is the fact that heretofore so-called cured cases will be handled better and longer and the ultimate results will be much more lasting.

Purposely, there has been avoided in this brief paper all the stereotyped signs and symptoms, which in text-books are attributed to this disease. They almost all stand for established tuberculosis. Incipient tuberculosis, much better called early tuberculosis, and the cases most hopeful of cure may require all the foregoing studies before arriving at a definite diagnosis; but so much depends on the proper solution of these cases, from a sociological point of view as well as industrial and economic aspects, that it is incumbent upon us not to treat these lightly or carelessly.

Some conclusions are: (1) the diagnosis of early curable tuberculosis is difficult at times; (2) suspicious cases should, if possible, be worked out to a confirmation by all means available; (3) the only tuberculosis of the lung that concerns us is active tuberculosis; (4) such diagnosis is best made by the general medical man; (5) an immediate diagnosis is sometimes impossible, and a statement made to the patient that you can find no active tuberculosis is an honest one, no matter what subsequent developments may occur.

THE INFLUENCE OF RENAL FUNCTION ON HYPERGLYCEMIA AND GLYCOSURIA IN DIABETES MELLITUS.

By Albert A. Epstein, M.D.,

ADJUNCT ATTENDING PHYSICIAN AND ASSISTANT PHYSIOLOGICAL CHEMIST, MOUNT SINAI HOSPITAL, NEW YORK.

(From the First Medical Service, Mount Sinai Hospital.)

The role of the kidney in the production and regulation of glycosuria still remains an unsettled problem. It is generally conceded that the presence of sugar in the urine usually represents an overflow from the blood. This assumption presupposes that the quantity of sugar in the blood is in excess of what the kidneys can tolerate or utilize, thereby causing its excretion. The point at which sugar begins to appear in the urine (threshold value) has not been definitely established. Numerous attempts have been made to ascertain the exact blood-sugar level which leads to glycosuria by means of oral and intravenous administration of glucose, but the results obtained thus far are not concordant. It is certain, however, that the kidneys of a normal individual are usually quite "impermeable" for the quantity of glucose that circulates in the blood even after the ingestion of large amounts of carbohydrates.

Increased Renal Permeability. Certain instances of glycosuria are on record in which an increase in the blood-sugar content above the normal percentage was not present, or rather not demonstrated. These cases have been variously termed "renal diabetes" or "renal glycosuria."[1] The phenomenon revealed by them is usually explained on the basis that the kidneys are more permeable to sugar than normally. In the light of recent work by the author,[2] the evidence adduced in proof of the existence of a renal diabetes or renal glycosuria cannot be regarded as wholly sufficient. It is yet to be determined that in these forms of glycosuria the "percentile" sugar content is the proper index of the actual amount of sugar in the blood.

The results of the investigation referred to point to the probability that the total sugar content of the blood plays the leading part in determining the presence or absence of a hyperglycemia and not its percentile concentration. According to this conception a hyperglycemia (increase in the total sugar content) may be present without showing any increase in the percentage of the blood-sugar. Because of this fact a glycosuria may even occur when the sugar content is apparently not increased. These phenomena appear in certain cases

[1] Lewis, D. S., and Mosenthal, H.: Johns Hopkins Bull., 1916, xxvii, 133.

[2] Epstein, Albert A.: Proc. Soc. Exp. Biol. and Med., 1916, xiii, 67; also, Relation of Hyperglycemia to Glycosuria, Monograph, May, 1916, New York.

of diabetes mellitus, and the following protocol is offered as an example.[3]

CASE HISTORY.—G. R.; female, aged forty-two years; admitted to the hospital (service of Dr. N. E. Brill) November 18, 1914. Chief complaints of patient: pruritus vulvæ, weakness, loss of weight, polydipsia, and polyuria. Exact date of onset of symptoms not known; but pruritus developed in summer of 1914, lasted a short time, and recurred two months prior to admission to the hospital. The polydipsia and polyuria were noted one month before the return of the pruritus.

Upon physical examination the patient appeared poorly nourished, with cheeks flushed, skin dry, and lips and tongue parched. A distinct acetone odor to the breath was present. Chest examination revealed the presence of a chronic bronchitis. Heart action was poor; no other cardiovascular phenomena. Abdomen lax; liver palpable below free border of ribs on deep inspiration. Marked redness of the vulva and the parts about. Cervix lacerated; uterus enlarged.[4]

On a mixed hospital diet the patient's urine contained from 2.1 to 4.2 per cent. of sugar, containing between 22 and 30 grams of glucose daily.

November 23, 1914, the blood-sugar and the relative blood volume were determined in the morning on a fasting stomach. Directly thereafter the patient was given a test breakfast of 50 grams of glucose in 200 c.c. of coffee. The blood-sugar, relative blood volume, and the urine were examined hourly for a number of hours. The results obtained are tabulated below.

TABLE I.

Time.	Blood-sugar, per cent.	Urine		
		Quantity, c.c.	Sugar, per cent.	Total sugar, grams.
9.30 A.M.	0.152			
10.30 A.M.	0.264	142	5.71	8.11
11.30 A.M.	0.184	62	5.45	3.38
12.30 A.M.	0.164	33	4.00	1.32
1.30 P.M.	0.116	17	1.54	0.26
2.30 P.M.	0.122	14	2.25	0.32
3.30 P.M.	0.138			

On a restricted diet the glycosuria disappeared very rapidly and the blood-sugar dropped to normal. The patient's general condition improved and the symptoms originally complained of were no longer present. The above test was repeated on December 2 and the following results were obtained.

[3] Epstein, Albert A.: Loc. cit.

[4] It was discovered subsequently that the patient was in the fifth week of pregnancy when she entered the hospital.

TABLE II.

Time.	Blood-sugar, per cent.	Urine		
		Quantity, c.c.	Sugar, per cent.	Total sugar, grams.
9.30 A.M.	0.080			
10.30 A.M.	0.121	47	0.30	0.141
11.30 A.M.	0.140	58	3.04	1.763
12.30 A.M.	0.125	47	4.36	2.049
1.30 P.M.	0.095	12	1.37	0.164
2.30 P.M.	0.076	25	0.30	0.075

The results yielded by the second test are of unusual interest and importance. It appears that the administration of the glucose in the test breakfast gave rise to an intense glycosuria, although the blood-sugar remained practically normal throughout the period of observation. At least the course pursued by the glycemia at this stage of the disease is comparable to that observed in cases of "renal diabetes."

After the subsidence of the glycosuria caused by the test there no longer appeared any sugar in the urine, although the diet was steadily made more liberal. The patient's condition continued to improve. On December 19, when the patient appeared to be in very good health and capable of tolerating liberal amounts of carbohydrates, another test similar to the one above was made, with the object of ascertaining the reaction of the blood and the kidneys to the administration of glucose. The results of this test appear in the table below.

TABLE III.

Time.	Blood-sugar, per cent.	Urine		
		Quantity, c.c.	Sugar, per cent.	Total sugar, grams.
9.30 A.M.	0.073			
10.30 A.M.	0.067	34	0	
11.30 A.M.	0.114	32	4.00	1.260
12.30 P.M.	0.127	98	4.36	4.273
1.30 P.M.	0.085	60	5.33	3.198
2.30 P.M.	.....	52	3.43	1.783

We observe here that the patient's blood-sugar on a fasting stomach reaches a low level, 0.075 per cent. No hyperglycemia is in evidence at any time during the entire test, at the same time that a very pronounced glycosuria is present.

I know of no case of "renal diabetes" in the literature in which so marked a glycosuria is present associated with so low a blood-sugar content. Without a definite knowledge of the antecedent history of this case, and the facts gleamed from the earlier tests, one might regard the case at this stage as an instance of "renal diabetes" or "renal glycosuria." The fact that the ingestion of glucose caused the glycosuria would not necessarily disbar it from this classification. The important feature is the absence of a hyperglycemia. If then the percentile blood-sugar content could be taken as the true index of the amount of glucose present in the blood the conclusion would be

warranted that the kidneys of this patient were or had become unusually permeable to sugar.

However, that the absence of hyperglycemia in the second and third tests made on this patient is only apparent and not real is evident from observations made on the blood volume simultaneously with the blood and urine analysis for sugar.[5] The data obtained show that the blood volume had become much increased, and, although the percentage concentration of glucose is low the total amount in circulation is increased throughout the glycosuric period. The increase in the blood volume that had occurred while the patient was under observation is demonstrated by the following results.

TABLE IV.—SHOWING CHANGES IN THE RELATIVE BLOOD VOLUME ON THE THREE TEST DAYS.

	Blood plasma, per cent.			Blood cells, per cent.			Relative blood volume, per cent.		
	Nov. 23.	Dec. 2.	Dec. 19.	Nov. 23.	Dec. 2.	Dec. 19.	Nov. 23.	Dec. 2.	Dec. 19.
9.30 A.M. . .	48.3	55.1	57.5	51.7	44.9	42.5	100.0	115.2	121.6
10.30 A.M. . .	51.8	55.2	60.9	48.2	44.8	39.1	107.4	115.2	132.2
11.30 A.M. . .	53.9	53.2	59.7	46.1	46.8	40.3	112.2	110.6	128.2
12.30 A.M. . .	53.8	56.3	59.9	46.3	43.7	40.1	111.9	118.6	128.9
1.30 P.M. . .	53.8	56.0	58.3	46.2	44.0	41.7	111.9	117.5	123.9
2.30 P.M. . .	56.2	56.0	59.7	43.8	44.0	40.3	118.0	117.5	127.7
3.30 P.M. . .	54.6	56.3	..	45.5	43.7	..	113.9	118.6	...

These data show very clearly just what has taken place in the circulating blood. Evidently its volume had increased, so that on December 2 and 19 it was found to be decidedly greater than it was at the time of the first examination on November 24. The percentages of sugar found in the blood upon examination are therefore masked by the alteration in the blood volume. Had the blood volume remained unchanged the blood-sugar content would really have been as follows:

TABLE V.—SHOWING THE CORRECTED BLOOD-SUGAR CONTENT ON THE THREE TEST DAYS.

	Blood-sugar		
	Nov. 23. Per cent.	Dec. 2. Per cent.	Dec. 19. Per cent.
9.30 A.M.	0.152	0.092	0.088
10.30 A.M.	0.283	0.134	0.089
11.30 A.M.	0.206	0.166	0.146
12.30 P.M.	0.183	0.147	0.164
1.30 P.M.	0.130	0.112	0.108
2.30 P.M.	0.144	0.090	
3.30 P.M.	0.158		

[5] The blood variations were determined by means of the simplified hematocrit devised by the author (Jour. Lab. and Clin. Med., 1916, i, 610).

According to my understanding of a hyperglycemia (*i. e.*, increase in the total blood-sugar content[6] these figures represent a definite hyperglycemia, and are compatible with the findings in the urine in the corresponding periods of time.

If we disregard the blood volume changes and their influence on the blood-sugar content in this instance we must draw the conclusion that the kidneys had become more permeable to glucose than they were at the outset, or that they had acquired the ability to eliminate sugar in the absence of a hyperglycemia. (Compare Tables I, II, III.) We would thus have a condition resembling renal glycosuria in a truly diabetic individual.

George Graham[7] records one case of definite diabetes with a relatively low blood-sugar content, and terms the condition "low-level leak-point." This observer, however, has made no control estimations of the blood volume in his case, and hence the interpretation given cannot be accepted as conclusive.

The occurrence of a glycosuria of purely renal origin is, of course, quite possible; but with the evidence which we possess concerning the phenomenon it seems premature to speak of the existence of "renal diabetes" or "renal glycosuria," or to regard the cases recorded in the literature as definite instances of increased renal permeability for glucose.

It appears fairly certain that changes in blood volume occur and that these changes exert an influence upon the concentration of different ingredients. It will therefore be necessary in the future in a consideration of the subject of hyperglycemia to take variations in blood volume into definite account. With the methods which we now possess for estimating blood-sugar and determining the blood volume there ought to be no difficulty in ascertaining whether or not a "renal glycosuria" or "diabetes" represents a condition of increased renal permeability or that such a glycosuria is the result of an actual (but masked) hyperglycemia.

Diminished Renal Permeability vs. Renal Tolerance for Sugar. A lessened capacity of the kidneys to eliminate sugar, on the other hand, is frequently encountered. The older observers (Naunyn,[8] v. Noorden[9]) as well as the more recent ones (Allen,[10] Macleod,[11] Graham,[12]) make mention of this condition, and numerous instances of persistent hyperglycemia with slight or no glycosuria are recorded. A number of such cases have come under my observation whose blood upon examination yielded the following results:

[6] Epstein, Albert A.: Loc. cit.
[7] Proc. Phys. Soc., London, Jour. Phys., 1916, xlix, 46–48.
[8] Der Diabetes Mellitus, 1906, p. 189.
[9] Handb. d. Path. d. Stoffw., 1907, ii, 7 and 9.
[10] Glycosuria and Diabetes, 1913, p. 48.
[11] Diabetes, its Pathology and Physiology, 1913, p. 48.
[12] Loc. cit.

TABLE VI.

Case.	Blood-sugar, per cent.	Urinary sugar, per cent.
1. G. Web	0.144	0
2. Re	0.195	0
3. Wur.	0.136	0
4. Str.	0.194	0
5. Lei.	0.154	0
6. Adv.	0.162	0
7. Feu.	0.208	0
8. Lev.	0.132	0
9. Gla.	0.324	0.25
10. Bon.	0.260	0
11. De B.	0.216	0
12. Rab.	0.164	0
13. Rub.	0.188	0
14. Mar.	0.324	0
15. Meh.	0.184	0
16. Fruh.	0.172	0
17. Bry.	0.222	0
18. Kay.	0.132	0
19. Sil.	0.190	0
20. Hor.	0.312	0
21. Pin.	0.196	0
22. Elie.	0.280	0
23. Le.	0.180	0
24. G. Car.	0.264	0
25. Ed. Car.	0.258	0
26. Gin.	0.180	0
27. Sche.	0.200	0

NOTE.—The blood was taken in all the above cases early in the morning, before breakfast, so that the figures represent the blood-sugar content on an empty stomach. The examination of the urine was made on twenty-four-hour specimens, on the same day on which the blood was examined.

The cases presented show varying degrees of hyperglycemia ranging from 0.132 per cent. to 0.324 per cent., without any glycosuria.

It is known that with the approach of coma in diabetes the sugar may disappear from the urine and accumulate in the blood. Clinical and experimental observations of this fact are on record. (v. Noorden,[13] Joslin,[14] Epstein and Felsen,[15] Epstein and Baehr.[16]) Extreme weakness and impaired circulation may also lessen or prevent the excretion of sugar because the kidney function is affected by these conditions.

In febrile states, too, the glycosuria may disappear while the hyperglycemia persists. According to Barrenscheen[17] the diminution or cessation of glycosuria after liberal feeding of oatmeal is due to diminished permeability of the kidneys. The relative infrequency of glycosuria in normal individuals after operative procedures (requiring the use of anesthetics such as nitrous oxide and ether) in whom a definite hyperglycemia develops is attributable to a lessened

[13] Loc. cit., p. 3.
[14] The Treatment of Diabetes, 1916, p. 72.
[15] AM. JOUR. MED. SC., to appear August, 1917.
[16] Jour. Biol. Chem., 1916, xxiv, 1.
[17] Biochem. Ztschr., 1912, xxxix, 232.

permeability of the kidneys.[18] The use or administration of a number of drugs and chemicals is known to affect the sugar-secreting power of the kidneys, and the development of a chronic nephritis is regarded as a common cause of the cessation of the glycosuria in diabetes. Thus, many conditions which affect the kidney function may interfere with the glycosuria.

But, whereas, the advent of a chronic nephritis may be associated with the disappearance of sugar from the urine, the latter need not necessarily be the result of the kidney affection. Very severe grades of renal disease may occasionally be present in diabetes without in any way interfering with sugar elimination. Two such cases have come under my observation, both dying of undoubted uremia.[19] In both the nephritis and the diabetes were of long standing; the glycosuria and hyperglycemia however, followed a course common to ordinary uncomplicated cases. The presence of albumin in the urine of diabetic individuals is very frequent, yet there appears to be no disturbance in the excretion of sugar in consequence of it.

The sugar may disappear from the urine of a diabetic without the intervention of a nephritis. According to Allen:[20] "The action of the sugar itself is held accountable for the diminished permeability of the diabetic kidney, and it would not be surprising if the kidney should acquire habituation to the long-continued hyperglycemia." A study of the blood-sugar and a close analysis of such cases points to the probability that the cessation of the glycosuria is in many of them the result of an altered state of carbohydrate assimilation rather than the sequel of a diminished renal permeability or sugar "habituation," for, we know that when an active disturbance of carbohydrate metabolism is present, causing a hyperglycemia and glycosuria, any interference with the excretion of sugar by the kidneys results in its accumulation in the blood. The disappearance of the glycosuria does not mark the cessation of the diabetes. This is confirmed by the progressive rise in the hyperglycemia. Clinical examples of this condition are furnished by the cases of Lepine,[21] v. Noorden, Joslin,[22] and also those of the author and Felsen.

Under these conditions the blood-sugar may rise to very unusual heights, 1 per cent. and over, the highest being 1.379 per cent. (Joslin[23]). Similar results are encountered in experimental animals after pancreatectomy (Epstein and Baehr[24]).

But this is entirely different from the conditions which exist in cases of diabetes, alluded to above (see Table VI), in which the glycosuria vanishes and a hyperglycemia persists without showing any progressive increase. Liefman and Stern[25] in their researches

[18] Epstein, A. A., Reiss, J., and Branower, J.: Jour. Biol. Chem., 1916, xxvi, 25.

[19] Case L. F.: Incoagulable nitrogen, 0.242 gm. per 100 c.c. serum. Case P. K.: Incoagulable nitrogen, 0.320 gm. per 100 c.c. serum.

[20] Loc. cit.

[21] Rev. de Méd., 1897, xvii, 832.

[22] Loc. cit., p. 72.

[23] Loc. cit., p. 72.

[24] Loc. cit.

[25] Biochem. Ztschr., 1906, i, 299.

on the subject have partly recognized this difference. In order to distinguish between the mechanism which governs the production of a hyperglycemia and that which regulates the glycosuria, they propose the terms "inner" and "outer tolerance" for sugar. The first term applies to the blood-sugar regulation and the ability of the tissues to use it. The second refers only to permeability of the kidneys.[26]

Without some such interpretation the conduct of the blood-sugar in the two types of cases is irreconcilable. Certainly, the term lessened "permeability" of the kidneys for sugar cannot be applied with equal propriety to both. A distinction must be made between the cases in which the disappearance of sugar from the urine results in a progressively increasing hyperglycemia and those in which the cessation of the glycosuria is accompanied by a persistent hyperglycemia which remains fairly constant. There is a clinical difference as well as a pathological one between the two groups: the one indicates failing renal function of a certain type, is rapid in its development, and often signifies the close approach of coma and death; the other is of long duration, often presenting none of the symptoms common to diabetes, and is compatible with good health.

In view of these facts I have applied renal function tests in addition to blood-sugar estimations to a number of cases of diabetes in order to determine the relation of the hyperglycemia and glycosuria to the activity of the kidneys. As stated before, Barrenscheen[27] in studying the influence of oatmeal feeding on the diabetes, found that the resulting decrease in the sugar output was associated with a disturbance in renal function which caused a retention of water and of glucose. Guided by the results of renal tests (lactose and potassium iodide) he came to the conclusion that the oatmeal caused an injury to the glomerulovascular apparatus. His deductions gain support from the fact that the administration of a diuretic, such as theocin, tends to overcome the effect of the oatmeal.

The results obtained in this investigation are therefore of considerable interest and serve to elucidate some of the points under discussion.

Methods. For the determination of renal function, phenolsulphonephthalein was used. Although this substance does not aid in distinguishing different types of renal affections it serves to indicate the presence and extent of functional disorders. An excretion of less than 60 per cent. of the dye in two hours is regarded here as subnormal. The blood-sugar was estimated by means of the microchemical

[26] In the 2 cases studied by Graham (loc. cit.) the phenomenon (hyperglycemia with little or no glycosuria, or "high—level leak—point" as he terms it) is interpreted as being of the "nature of a protective mechanism." But it is difficult to understand the meaning of "protective mechanism." Does it signify diminished renal permeability or altered carbohydrate utilization?

[27] Barrenscheen, H. K.: Loc. cit.

method of the author,[28] and for quantitative analyses of the glucose in the urine, Rudisch solution was employed.

The observations here recorded were carried out on 60 cases. The blood was obtained for analysis early in the morning on a fasting stomach. Directly thereafter the patients received 6 mgs. of phenolsulphonephthalein intramuscularly and then were permitted to drink 2 glasses (16 ounces) of water. The patients voided urine at the end of one and two hours. In certain instances the urine was obtained by catheterization. In a number of cases the examination was repeated, for reasons which will be evident later on.

The cases studied may be grouped as follows:

1. Active cases of diabetes untreated:
   (*a*) Without renal disease.
   (*b*) With renal disease.
2. Active cases of diabetes rendered sugar-free by treatment:
   (*a*) Without renal disease.
   (*b*) With renal disease.
3. Confirmed cases of diabetes which have become sugar-free spontaneously:
   (*a*) Without renal disease.
   (*b*) With renal disease (none encountered).
4. Active cases of diabetes showing diminution or disappearance of the glycosuria, but in reality the condition being much aggravated.

TABLE VII.—GROUP I.—UNTREATED CASES OF DIABETES, WITHOUT NEPHRITIS.

Case.	Blood-sugar, per cent.	Urine. 24-hr. specimen, c.c.	Urine. Sugar, per cent.	Phenolsulphonephthalein. 1st hr., per cent.	Phenolsulphonephthalein. 2d. hr., per cent.	Excretion, total per cent.
23. M. Le.	0.210	3000	2.0	38.0	26.0	64.0
28. Mas..	0.210	2350	4.1	55.0	26.0	76.0
29. Nat.	0.300	2250	5.0	48.0	18.0	66.0
30. Ros.	0.292	2750	4.1	50.0	15.0	65.0
Average	0.253		3.8			68.0
UNTREATED CASES OF DIABETES WITH NEPHRITIS.						
9. Gla.	0.324	..	0.25	23.0	28.0	51.0
22. Elie	0.252	..	0.75	13.0	20.0	33.0
10. Bon.	0.260	..	0.40	29.0	18.0	47.0
21. Pin.	0.248	1325	1.40	27.0	13.0	40.0
Average	0.271		0.70			43.0

The figures tabulated above are representative of the results obtained in a large number of diabetic patients upon whom the tests were made prior to the inception of treatment. The table shows that the range of variation of the hyperglycemia in the two types of cases is approximately the same, but the extent of the glycosuria is strikingly different. Comparison is facilitated by averaging the

[28] Epstein, Albert A.: Jour. Am. Med. Assn., 1914, lxiii, 1667.

figures obtained. We thus find that the blood-sugar content in the two groups is 0.258 per cent. and 0.271 per cent.; whereas the concentration of the urinary sugar is 3.71 per cent. and 0.70 per cent., respectively. The phenolsulphonephthalein excretion of these cases seems to parallel the sugar elimination, being considerably lower in the nephritic than in the non-nephritic group, the average for the two groups being 66 per cent., and 43 per cent., respectively.

It would appear from a comparison of the phenolsulphonephthalein excretion and the sugar output of the cases presented that there is a definite relation between the two functions: that disease of the kidneys interferes with the sugar elimination as well as with that of the dye. In view of the approximate equality of the hyperglycemias in the two types of cases and the marked difference in the glycosuria it would seem likely that the kidneys of the nephritic individuals are less permeable to sugar than those of the non-nephritic cases.

However, it does not necessarily follow that the diminished glycosuria observable in the nephritic cases is the result of the renal disease. In the first place, repeated examinations of the blood-sugar in the nephritic cases fails to show any progression of the hyperglycemia, such as that found in cases in which failing kidney function interferes with the elimination of sugar (see Cases 35 and 36); so that the hyperglycemia observed in these nephritic cases is really not the result of sugar retention due to renal "impermeability." Further, withdrawal of carbohydrates from the diet of these individuals leads to a rapid disappearance of the glycosuria, but the hyperglycemia persists. Reference has also been made to the fact that a very severe nephritis may be present and exert no influence whatever on the intensity of the glycosuria nor on the height of the hyperglycemia. For example the two cases of this type previously mentioned presented the following results:

Case A. F. Blood-sugar, 0.300 per cent.; urine, 4440 c.c.; sugar, 5 per cent.; total, 222 grams. Phenolsulphonephthalein, 18 per cent.

A. K. Blood-sugar, 0.218 per cent.; urine, 3600 c.c.; sugar, 4.6 per cent.; total, 165.6 grams.

The quantity of sugar found in the blood at any one moment represents the result of three functions: (1) the rate at which sugar is thrown into the circulation; (2) the rate of its utilization by the tissues; (3) the rate of renal excretion. If the supply of sugar to the blood is in excess of tissue requirement, and more than the kidneys can eliminate, it must accumulate in the blood stream. This has been referred to above and will be demonstrated by specific cases presently. If, therefore, a marked hyperglycemia is present which remains constant over a considerable period of time, causing little or no glycosuria (whether a nephritis is present or not), it signifies that a balance has been established between the rate at

which sugar is supplied to the blood and its utilization by the tissues. This is supported by the findings in a group of cases without renal disease in which the glycosuria disappeared spontaneously or following treatment, but the hyperglycemia remained persistently high. (See Tables VIII and IX.)

TABLE VIII.—GROUP II.—DIABETIC CASES RENDERED SUGAR-FREE BY TREATMENT: NON-NEPHRITIC.

Case.	Blood-sugar, per cent.	Urine. 24-hr. specimen, c.c.	Urine. Sugar, per cent.	Phenolsulphonephthalein. 1st hr., per cent.	Phenolsulphonephthalein. 2d. hr., per cent.	Excretion, total per cent.
25. Ed. Car.	0.258	1560	0	40.0	22.0	62.0
31. A. Mor.	0.178	1250	0	44.0	27.0	71.0
17. Bry	0.222	..	0	40.0	22.0	62.0
16. Fruh.	0.172	3000	0	57.0	21.0	78.0
14. Mar.	0.324	..	0	60.0	15.0	75.0
15. Meh.	0.182	..	0	..	..	69.0
24. G. Car.	0.264	1600	0	54.0	21.0	75.0
11. De B.	0.216	..	0	33.0	23.0	56.0
5. Lei	0.164	2500	0	30.0	29.0	59.0
Average	0.220					67.0

DIABETIC CASES RENDERED SUGAR-FREE BY TREATMENT: NEPHRITIC.

7. Feu.	0.208	..	0	17.0	24.0	41.0
20. Hor.	0.312	..	0	26.0	29.0	55.0
32. Trou.	0.101	900	0	37.0	9.0	46.0
33. J. Wei.	0.213	..	0	28.0	27.0	55.0
Average	0.217					49.0

TABLE IX.—GROUP III.—CONFIRMED DIABETICS WHO HAVE BECOME SUGAR-FREE SPONTANEOUSLY: NON-NEPHRITIC.

Case.	Blood-sugar, per cent.	Urine. 24-hr. specimen, c.c.	Urine. Sugar, per cent.	Phenolsulphonephthalein. 1st hr., per cent.	Phenolsulphonephthalein. 2d. hr., per cent.	Excretion, total per cent.
19. Sil.	0.196	1500	0	55.0	19.0	74.0
18. Kay.	0.132	..	0	40.0	30.0	70.0
6. Adv.	0.162	..	0	47.0	17.0	64.0
4. Str.	0.194	2280	0	42.0	18.0	60.0
Average	0.171					67.0

Among the cases presented in Table VIII there are four with evidences of renal disease. The only difference observable between these latter and the non-nephritic cases is in the amount of phenolsulphonephthalein excreted. The non-nephritic cases manifest a high blood-sugar content without a glycosuria and the phenolsulphonephthalein elimination is normal. The group of spontaneously recovered cases is comprised of individuals who were known to have had diabetes but who made no special effort to control the disease. From the stand-point of the glycosuria these cases

might be classed as mild or moderate. However, the blood-sugar in them is high, but not to the same extent as in those which have been rendered sugar-free by treatment. This may be due to a difference in the duration of the sugar-free period. The functional activity of the kidneys in these cases is perfectly normal.

Two deductions appear admissible from these results: (1) that an increased blood-sugar content may be present in diabetic individuals without giving rise to glycosuria even in the absence of renal disease; (2) that the hyperglycemia in the nephritic individuals is no greater than it is in the non-nephritic.

That the hyperglycemia observed in the above cases is not the result merely of a lessened renal permeability, but that of some alteration in the supply and utilization of sugar, is shown by the relative constancy of blood-sugar content which is observed when the examinations are frequently repeated. An illustration of this fact is found in the following cases:

TABLE X.

Case.	Date.	Blood-sugar, per cent.	Urine-sugar.
2. Re.	Jan. 29, 1916	0.195	0
	Nov. 1, 1916	0.220	0
	Nov. 11, 1916	0.180	0
5. Lei.	July 13, 1916	0.154	0
	July 31, 1916	0.148	0
	Aug. 5, 1916	0.162	0
10. Bon.	April 8, 1916	0.260	0
	April 9, 1916	0.244	0
	April 10, 1916	0.250	0
	April 11, 1916	0.260	0
	April 12, 1916	0.210	0
	April 13, 1916	0.200	0
	April 14, 1916	0.220	0
	April 16, 1916	0.240	0
22. Elie.	June 19, 1916	0.280	0
	July 8, 1916	0.320	0
	July 15, 1916	0.320	0

The above cases serve as an illustration of the condition which is encountered in certain cases of diabetes—namely, a persistent hyperglycemia which remains at a constant level. There is no glycosuria, notwithstanding the fact that the kidneys functionate normally in all other respects. From what has been said before we must conclude that a rearrangement of some sort has taken place by which a balance between the supply of sugar to the blood and its utilization by the tissues is constantly maintained. Undoubtedly, the kidneys take part in this process, as other organs do, so that the absence of sugar from the urine does not indicate a lessened permeability (in the sense of inability to eliminate glucose or an active interference with its excretion), nor does it signify "habituation" of the kidneys to the hyperglycemia, for that alone would not be capable of maintaining the blood-sugar content at a constant level.

We must assume, therefore, that the hyperglycemia without a glycosuria which we find in these cases represents a condition in which the supply of sugar is appropriate to the utilization and does not exceed it. The acquired "tolerance" of the kidneys for the hyperglycemia in this sense constitutes a "protective mechanism" (see footnote 26, p. 110) and is different from the mechanism ordinarily understood in the term "lessened permeability."

When the supply of sugar to the blood exceeds the rate of its utilization by the tissues the result is a hyperglycemia. What actually happens when the kidneys fail to excrete the excess is that it accumulates rapidly in the blood and the hyperglycemia mounts progressively. This is illustrated by the cases already referred to (Lepine, v. Noorden, etc.), and the experiments on animals (Epstein and Baehr) mentioned above.

It also has been pointed out that the presence of renal disease and reduced phenolsulphonephthalein excretion may be associated in diabetes, with a marked hyperglycemia and slight glycosuria, and that the latter is not necessarily the result of the nephritis. The question therefore arises concerning the nature of the renal disturbance which is capable of interfering with the glucose elimination, in consequence of which the liberated and unused sugar accumulates in the blood. Reference has been made to Barrenscheen's observations on the effect of oatmeal on the sugar secreting function of the kidneys. The disturbance produced is evidently of a circulatory nature. This is supported by the tests with lactose and potassium iodide instituted by him and by the salutary effect of diuretics upon the disturbance.

The following protocols are therefore of special interest in this connection, because they demonstrate the role of the kidneys in the regulation of the hyperglycemia and glycosuria in diabetes. They indicate, furthermore, that "lessened permeability" is probably identical with failing renal function of a type which may react to therapeutic measures.

GROUP IV.

CASE 35.—A. K.; male; aged sixty-three years; suffering from diabetes mellitus for eighteen years. One week before coming under observation he developed a thrombosis of the femoral artery. Upon examination it was found that the patient had a chronic endocarditis and arteriosclerosis. The urine was small in amount (daily output about 900 c.c.), highly concentrated, and contained a moderate amount of albumin, numerous casts, and some blood cells. The sugar output ranged from 2.0 per cent. to 3.5 per cent. The blood-sugar varied between 0.220 and 0.260 per cent.

Dietary restriction (modified Allen regime) caused a prompt disappearance of the glycosuria. The patient's condition improved and he was gradually allowed more food. Two weeks after the

first observation, when the patient was permitted to sit in a chair, it was noticed that the quantity of urine passed became diminished (660 c.c. per day). It remained sugar-free, but the amount of albumin and formed elements increased. The heart action appeared much weaker, but there was no evidence of cardiac enlargement. The healthy extremity showed slight edema. The blood examined at this time showed a hyperglycemia of 0.412 per cent.

It was evident that the patient at this stage was receiving more carbohydrate than he could tolerate, and because of the circulatory disturbance, which also affected the kidneys, no sugar appeared in the urine. Cardiac stimulation was resorted to (spartein sulphate and infusion of digitalis), with very prompt response in the pateint's condition. The heart action improved; the quantity of urine rose to 1500 c.c. Sugar appeared in the urine (2.2 per cent.) and the blood-sugar dropped to 0.200 per cent.

CASE 36.—A. M.; female, aged forty-two years. Came under observation February 16, 1916, with a history of menorrhagia and diabetes mellitus. Patient stated that when the urine was first examined (some time in January) it contained over 10 per cent. of glucose. The patient complained of the usual symptoms, particularly of the polydipsia and the pruritus vulvæ, both of which were observed one month prior to the date of consultation. Upon examination the patient appeared emaciated, weighing 110 pounds (usual weight 139 pounds). The skin and mucous membranes were dry. Tongue heavily coated; acetone odor to the breath. Heart action rapid (110 beats per minute); sounds fairly good; no murmurs. Pulses small and soft; blood-pressure 112 systolic and 80 mm. diatolic (Merser apparatus). Abdomen lax; liver not enlarged. Marked hyperemia of the vulva; uterus enlarged; tumor mass palpable in the posterior wall.

The patient was put on a restricted diet: 500 grams of 5 per cent. vegetables, black coffee, broths, and small amounts of whisky, 1 to 2 ounces daily. This diet was kept up until the patient became sugar-free, and then gradual additions of other foodstuffs were made.

The clinical course pursued by the patient during the first period of observation (February 16 to March 7), was very favorable. Although there occurred a progressive loss in weight, there seemed to be general improvement. The symptoms originally complained of disappeared and the patient experienced a feeling of well-being. The changes which took place in the blood and urine are recorded in Table XI.

February 17, the first day of observation, the patient eliminated 2000 c.c. of urine, containing 1.2 per cent. of glucose. The blood-sugar was 0.220 per cent., and the phenolsulphonephthalein excretion was 74 per cent. in two hours. March 4 another phenolsulphonephthalein test was made and the excretion was normal (71 per cent.

in two hours), although the blood-sugar was 0.178 per cent., and the urine was sugar-free. In other words, the hyperglycemia which remained was not associated with any disturbance of renal function.

TABLE XI.—CASE 36.

Date.	Urine.		Acetone.	Diacetic acid.	Blood-sugar, per cent.	Alveolar CO_2.	Phenolsulphonephthalein excretion.			Remarks.
	Quantity, c.c.	Sugar, per cent.					1st hr.	2d hr.	Total	
							p. c.	p. c.	p. c.	
Feb. 16, 1916	S.S.	+	+++	+++						
" 17, 1916	2000	1.2	++	++	0.220	..	46	28	74	
" 18, 1916	1500	0.8	++	+						
" 19, 1916	1875	0.6	+	0						
" 20, 1916	1575	0.55	+	++						
" 21, 1916	1950	0	+	0						
" 22, 1916	1600	0	VFT.	0						
" 23, 1916	1375	0	+	0						
" 24, 1916	1250	0	VFT.	0						
" 25, 1916	1200	0	VFT.	0						
" 26, 1916	1600	0	VFT.	0						
" 27, 1916	1200	0	+	0						
" 28, 1916	1400	0	+	0						
" 29, 1916	2150	0	VFT.	0						
Mar. 1, 1916	1600	0	++	0						
" 2, 1916	1125	0	+	0						
" 3, 1916	850	0.7	+	0	0.196					
" 4, 1916	1250	0	+++	0	0.178		44	27	71	
" 5, 1916	750+	0	FT.	0						
" 6, 1916	2725	0	VFT.	0						
" 7, 1916	1200	0.55	+	0	0.182					
June 7, 1916	1200	0.25	+	0	0.284	5.6				
" 8, 1916	1120	0	+	FT.						
" 9, 1916	840+	0.43	Tr.	0	0.268	6.0			48	
" 21, 1916	1080	0.2	0	..	0.288	5.1				
" 22, 1916	990	0	0	0	0.324	3.2				
" 25, 1916	1020	0	0	0	0.272					
July 4, 1916	690	0	0	0	0.166	4.2	..	..	34	Edematous.
" 5, 1916	8000	0	0	0	..	..	..	..	..	Inf. digitalis.
" 6, 1916	3500	0	0	0	0.356	..	..	..	..	Edema absent.
" 7, 1916	2400	0.5	+							
" 10, 1916	1980	2.5	++	Tr.						
" 11, 1916	960	2.2	++	+						
" 12, 1916	1320	2.0	++	+						
" 13, 1916	1440	2.0								
" 19, 1916	1500	1.66								
" 21, 1916	1650	1.1	++	0	0.206	3.9			71	

+ = decided reaction. VFT. = very faint trace. FT. = faint trace. Tr. = trace. Inf. = infusion. S.S. = single specimen.

In the interval between March 7 and June 7 the patient was seen infrequently and definite observations could not be made. June 7 the patient returned and appeared to be in very poor condition. The urine contained only 0.25 per cent. of glucose, a trace of acetone, and no diacetic acid. The blood-sugar, however, was 0.284 per cent., the highest figure yet attained in this case. On the following day the urine was again sugar-free, but a day later a small quantity of sugar reappeared (0.43 per cent.). The blood-sugar taken then was 0.268 per cent., and the phthalein excretion was only 48 per cent. in two hours, hence much lower than in the previous test. It is evident from this observation that there was a retention of sugar at the time, occasioned by defective function, and consequent decrease in renal permeability.

A slight glycosuria alternating with a sugar-free state continued until June 20. The blood-sugar remained at approximately the same high level. In view of the patient's very low tolerance for carbohydrates (in fact for any food) it appeared advisable to attempt fasting. The result of this procedure was an aggravation of existing conditions. The urine became free from sugar and ketone bodies, but the blood-sugar rose to 0.324 per cent., a still higher level than previously observed. The acidosis also increased, as shown by the alveolar CO_2, which dropped to 3.2 per cent. (Frederici apparatus).

A further rise in the hyperglycemia showed definite progression of the diabetic process, notwithstanding the fact that the urine was sugar-free. The fasting was therefore interrupted. A small quantity of 5 per cent. vegetables was allowed, together with 500 c.c. of milk and two ounces of whisky. Because of the increasing acidosis, bicarbonate of soda (4 grams t. i. d.) was administered. As a result of this treatment the patient's condition seemed to improve. The urine remained free from sugar and acetone and the blood-sugar dropped to 0.272 per cent. It is noteworthy that the daily output of urine in this period has been small, particularly as the thirst and polydipsia were pronounced.

The existing pathological conditions became apparent from the course of events in the next period of observation (July 3 to 21). July 3, contrary to instructions, the patient took a lengthy automobile ride. Before the completion of the trip the patient suddenly became very faint, and upon her return it was found that she seemed swollen all over. A very pronounced general anasarca developed in the next twelve hours. The heart action was slow (48 beats per minute) and feeble. The respirations were slow (12 per minute) and sighing in character. The patient was very drowsy, but responded to questions when aroused.

The urine was sugar-free and did not contain any ketones. The blood-sugar was only 0.166 per cent. The phthalein excretion was 34 per cent. in two hours. The latter, of course, was in keeping with the clinical phenomena, *i. e.*, reduced urinary excretion and the edema, but the relatively low hyperglycemia appeared to be paradoxical. The absence of glycosuria, because of deficient renal permeability, should have caused a retention of sugar in the blood, and hence a greater hyperglycemia. The reason for this discrepancy appears in the developments of the next few days.

Following the therapeutic indications at this stage the bicarbonate of soda was stopped, and the infusion of digitalis, in half-ounce doses, every three hours was administered. The result was most remarkable. In the ensuing twenty-four hours the patient eliminated 8000 c.c. urine, which was free from sugar, acetone, and diacetic acid, and the day following 3500 c.c. of a like urine was passed. The edema disappeared entirely. The blood-sugar examined on the morning of July 6 showed the high figure of 0.356 per cent. The blood-pressure, systolic, rose to 128 mm. The heart

action was more forcible and the pulse-rate 68 per minute. With the improvement in renal secretion, sugar reappeared in the urine, at first 0.5 per cent. (July 7), rising gradually to 2.5 per cent. (July 10). Subsequently it diminished slowly, and on July 21 the glycosuria was only 1.1 per cent. The blood-sugar on that day was only 0.206 per cent. The phthalein test showed again a normal excretion (71 per cent. in two hours).

Thus it appears that during the period of anasarca the lowered hyperglycemia was due to abstraction of sugar from the blood by the edema fluid. With the increased diuresis and the subsidence of the edema the surplus sugar was returned to the blood. Sugar did not appear in the urine until the function of the kidneys improved, and the glycosuria became progressively more intense as renal activity increased. Following the elimination of the retained sugar the hyperglycemia diminished, so that finally when the renal function returned to normal (July 21) we find moderate glycosuria with a corresponding hyperglycemia, comparable to that observed on the day of the first test (February 17).

The above cases (unlike those of Groups 2 and 3, *vide supra*) show that interference on the part of the kidneys with elimination of sugar causes a retention of this substance in the blood, and hence a progressively increasing hyperglycemia. Although we have no conclusive evidence of the exact nature of the renal disturbance which affects the glycosuria and hyperglycemia in this manner, the associated circulatory disturbances make it seem probable that the derangement in the kidneys is of circulatory origin analogous to the condition found after feeding oatmeal (Barrenscheen). The prompt manner in which these cases react to cardiovascular stimulation, with an increase or reappearance of the glycosuria and a fall in the hyperglycemia, makes this deduction all the more likely.

These observations are of importance not only in showing us a phase of kidney function which influences the hyperglycemia and glycosuria, but also because the diminution or cessation of glycosuria in diabetes mellitus, which is accompanied by a progressively increasing hyperglycemia, affects the prognosis and constitutes an important indication for certain therapeutic measures.

We thus encounter two types of cases in diabetes: one in which the disappearance of the glycosuria is associated with a definite retention of sugar in the blood, due to failing kidney function (lessened permeability), which is probably of circulatory origin; the other in which the cessation of the glycosuria is not the result of renal interference. In this latter group the hyperglycemia may persist, but it remains constant—at least it shows no progression. That this is due to a rearrangement of the carbohydrate metabolism, whereby the plane of sugar utilization becomes elevated ("inner tolerance" of Liefman and Stern or "protective mechanism" of Graham), and not due to a lessened renal permeability, is gleaned from the conduct of such cases under special conditions of nutrition.

Since the introduction of the fasting method of treatment of diabetes we have found that the ordinary uncomplicated cases (particularly those of recent origin) show that the disappearance of glycosuria is accompanied by a rapid fall in the blood-sugar, often reaching the normal level. In the group of cases mentioned above (Group 2), fasting reduces the hyperglycemia somewhat, but does not, as a rule, bring it back to normal. In a small proportion of cases considerable reduction in the hyperglycemia may thus be obtained. Macleod mentions one case[29] in which the blood-sugar decreased from 0.183 per cent. to 0.107 per cent., after rigid dietary control. I have found among my cases thirteen instances of reduced hyperglycemia following adequate dietary management, ranging over varying periods of time (see Table XII).

In most instances, however, the hyperglycemia persists long after the disappearance of the glycosuria, notwithstanding fasting and prolonged dietary restrictions.

TABLE XII.

Case.	Date.	Blood-sugar, per cent.	Urine-sugar.
6. Adv.	July 17, 1916	0.162	0
	July 26, 1916	0.066	0
	Aug. 30, 1916	0.098	0
19. Sil.	May 31, 1916	0.196	0
	June 19, 1916	0.115	0
	July 3, 1916	0.080	0
4. Str.	July 16, 1916	0.194	0
	July 30, 1916	0.094	0
	Sept. 8, 1916	0.116	0
	Sept. 21, 1916	0.105	0
32. Trou.	Oct. 28, 1915	0.164	0
	Aug. 24, 1916	0.101	0
25. Ed. Ca.	Jan. 3, 1916	0.300	0
	Nov. 7, 1916	0.194	0
	April 17, 1916	0.258	0
	Aug. 23, 1916	0.162	0
15. Meh.	June 6, 1916	0.182	0
	Aug. 15, 1916	0.100	0
7. Feu.	June 19, 1916	0.208	0
	Aug. 30, 1916	0.112	0
	Sept. 25, 1916	0.110	0
16. Fruh.	July 17, 1916	0.172	0
	Aug. 16, 1916	0.136	0
5. Lei.	July 10, 1916	0.164	0
	Sept. 2, 1916	0.142	0
	Sept. 8, 1916	0.104	0
	Sept. 28, 1916	0.103	0
27. Sche.	Nov. 6, 1914	0.200	0
	May 15, 1916	0.075	0
2. Re.	Jan. 15, 1916	0.260	0
	Jan. 29, 1916	0.195	0
	Nov. 11, 1916	0.180	0
21. Pin.	April 1, 1916	0.248	0
	April 8, 1916	0.196	0
34. Toc.	Sept. 19, 1915	0.190	0
	Sept. 16, 1916	0.109	0

[29] Macleod, J. J. R.: Loc. cit.

SUMMARY AND CONCLUSIONS. 1. A condition simulating renal diabetes, *i. e.*, a glycosuria without hyperglycemia, may occur in diabetes mellitus. This is brought about by an increase in blood volume which reduces the concentration of the blood-sugar, and the consequent fall in its percentage masks the hyperglycemia. In order, therefore, to prove the existence of a true renal diabetes it is necessary to show that the total sugar content of the blood is not increased above normal.

2. Hyperglycemia without glycosuria is of frequent occurrence in diabetes mellitus. When sugar is absent from the urine a persistent hyperglycemia which remains constant or does not show progression indicates an altered state of carbohydrate metabolism in which a balance is established between the supply of sugar to the blood and its utilization by the tissues on a higher plane than that found normally. This is interpreted as a condition of increased "tolerance" of the kidneys for sugar and not that of "lessened permeability."

3. Renal disease (true nephritis) need not interfere with the elimination of sugar. The cessation of the glycosuria in diabetes mellitus when a nephritis supervenes is not necessarily the result of the kidney affection. Increased tolerance of the kidney for sugar may exist when a nephritis develops. The two conditions may be synchronous or coincident.

4. Lessened permeability of the kidneys, *i. e.*, interference with the excretion of sugar in the course of an active diabetes, leads to the progressive accumulation of sugar in the blood. The glycosuria may diminish or disappear entirely. This clinical complex portends the approach of coma and appears to be due to a circulatory disturbance of the kidneys associated with a general cardiovascular asthenia. The administration of appropriate medication may overcome the disorder. Improvement manifests itself by reappearance of the glycosuria, with a consequent fall in the hyperglycemia. The development of an anasarca may cause a fall in the percentile blood-sugar content and thus conceal the retention of sugar. This is due to the abstraction of sugar from the blood by the edema fluid. The subsidence of the anasarca causes a return of the hyperglycemia.

5. Testing the kidney function by means of phenolsulphonephthalein in diabetes mellitus is a useful procedure. It aids in understanding the relation of the hyperglycemia to glycosuria. It is particularly helpful in those cases in which a fall in the urinary sugar is associated with a rise in the blood-sugar, thus yielding confirmatory evidence of the fact that the elimination of glucose is interfered with.

I wish to acknowledge my thanks to Dr. Joseph Reiss for technical assistance in the work.

REVIEWS

FRACTURES AND DISLOCATIONS. By L. A. STIMSON, B.A., M.D., LL.D. Yale; Professor of Surgery in Cornell University Medical School, New York; Consulting surgeon to New York and Bellevue Hospitals, etc. Eighth edition. Pp. 946; 475 illustrations and 39 plates. New York and Philadelphia: Lea & Febiger, 1917.

THE fact that this is the eighth edition of the excellent work is insurance enough of the value of its text and the appreciation of its work by the profession at large.

The principal changes and additions in the work are in the line of treatment. In recent years there has been marked increase in the interest taken in fracture treatment. The great number of fractures treated among the soldiers has also added much to the available knowledge of the more obscure points. The author in two visits to France saw a great deal of the fracture work done by many of the ablest surgeons in the world and has consequently enhanced the value of his work by such additions.

The book describes in detail many of the newer forms of suspension and extension treatment of fractures both simple and compound. Illustrations of such dressings are included and add greatly to the value of the text in that they show us the important details accurately. Throughout the work, the treatment is given great consideration and no minutiæ is too unimportant to describe. This is a very good principle, for so many books on fractures neglect this very vital point. Furthermore, great stress is justly and wisely laid upon traction and extension as a very important feature in certain types of injury.

In the chapters on dislocations, the largest addition has been on the subject of the dislocations of the shoulder in infancy—birth dislocations and the posterior subluxations. A short section on subluxation of the great horn of the hyoid has also been added.

The work is an exceedingly valuable one by virtue of its completeness, lucidity of detail and great number of good descriptive illustrations.

E. L. E.

SURGICAL OPERATIONS. By KRAUSE, HEYMAN and EHRENFRIED. Vol. II. Pp. 715; 373 illustrations. New York: Rebman Company, 1917.

THIS volume, the second of a series of six, deals with the surgical operations on the jaws, the mouth, pharynx, salivary glands, facial and cervical nerves, and brain. It is written in German primarily and translated into English by Albert Ehrenfried. The book is larger than need be, due to wasted space in wide margins and unnecessarily large illustrations. Although the authors designate the work as one of surgical operations, they consume lots of valuable space with daily clinical notes on their operative cases in many instances. They also devote too great description of network of veins, small arteries, etc., that they mention but only to suggest their probable identity. These digressions are very helpful and exceedingly interesting from the clinical standpoint, but tend to make an operative surgery too cumbersome.

With these exceptions the work is a very good one. The text is clearly pleasing, presented despite a definite inclination toward the foreign style of expression. The plates are excellently executed in color and are very descriptive of the point they intend to depict.

The volume is really much more than are operative surgery. In addition to describing the operations in more or less detail, it takes up the clinical phase and also refers repeatedly to other author's works.

Many of the operations described are but seldom seen so that the book really brings us something almost entirely new in many respects. E. L. E.

A TEXT-BOOK OF HISTOLOGY. By FREDERICK R. BAILEY, A.M., M.D. Fifth edition. Pp. 652; 392 illustrations. New York: William Wood & Co.

THE present edition shows but slight changes from the previous one, reviewed in this JOURNAL, 1915, vol. cl., p. 130. The demand for a new printing shows that the book has attained a place among standard tests for the instruction of students in normal histology. The chapter on the central nervous system by Dr. O. S. Strong, containing a little over 100 pages, is quite comprehensive. It gives not only the histology of important regions, but also descriptions and illustrations of cross-sections of the brain stem at various levels, and diagrammatic charts to show the course of the more important pathways. To anyone desiring a succinct and well-balanced account of the internal structure of the nervous system, a study of this presentation of the subject will be interesting. W. H. F. A.

THE PATHOLOGY OF NEPHRITIS. By WILLIAM OPHÜLS, Division of Pathology, Stanford University Medical School. Pp. 103; 64 photographs and photomicrographs. Published by the Stanford University, California.

THIS small book consists of a record of thirty-two cases of acute, subacute and chronic glomerulonephritis. Of each case a brief clinical history, the urinary findings, the blood-pressure, eye-ground findings and in some case phthalein tests are given. A detailed description of the gross and histologic pathology of the kidney follows the clinical record and a microphotograph of the kidney of each case is included. The author discusses the cases in four groups: acute, early subacute, late subacute and chronic cases, and draws certain conclusions from the series.

As a collection of carefully studied cases the book is of much interest to the investigator in renal pathology and might serve a useful purpose in furnishing the student with a larger series of cases of these types of nephritis than he would be likely otherwise to have presented to him. J. H. A.

BONE AND JOINT STUDIES. By LEONARD W. ELY, Associate Professor of Surgery (Orthopedics), and JOHN FRANCIS COWAN, Assistant Professor of Surgery in Stanford University. Pp. 139; 41 illustrations: Stanford University Publications.

THIS pamphlet presents the results of experimental work by the authors on dogs and rabbits in connection with the following subjects: Experimental resection of the dog's knee-joint; reaction of the tissues of the knee-joint of the rabbit to injury; a study of one hundred dry bones sawed in the laboratory; a study of the sterno-clavicular joint. A summary of each experiment is given and conclusions are presented at the termination of each piece of work.

T. T. T.

PRINCIPLES OF TREATMENT OF BROKEN LIMBS. By WILLIAM F. FLUHRER, Consulting Surgeon to Bellevue and Mount Sinai Hospitals. Pp. 122; 31 illustrations. New York: Rebman Company.

BEGINNING in 1872, while a member of the House Staff of the Bellevue Hospital of New York, the author devised a method for the more speedy fixation of the fragments of a fracture in adjusted relations. This was accomplished by means of the use of roughened narrow tin strips and plaster-of-Paris bandages for the construction of the permanent retentive apparel. Special emphasis is given to

the author's apparatus for the setting and fixation of the fragments of a fracture of the femur. Its inexpensiveness, ease of construction and apparent effectiveness, call for special consideration now in view of the great difficulties to be met with in the treatment of such fractures under war conditions. Open operation in simple fractures, septic wound complications, compound fractures and primary amputations, receive especial attention T. T. T.

A Practical Medical Dictionary. By Thomas Lathrop Stedman, A.M., M.D. Fourth revised edition. Pp. 1102; illustrated. New York: William Wood & Co.

The reviewer had the opportunity of reviewing a previous edition of this work, the second; at that time the dictionary, from a rather hasty perusal of its contents, was spoken of in extremely commendatory terms. Since then this second edition has been in constant use. During the past four years but three words were found in the literature which upon referring to the book were not incorporated in it. In the present edition, the fourth, the reviewer finds not only these three words but also more than two thousand others!—a splendid commentary of the additions that have been made. After all the *sine qua non* of a dictionary is the number of definitions, and in the present volume the writer has been unable to find any words omitted. As to the correctness of the spelling, the character of the definitions themselves, and the pronunciation of the words, the name of the scholarly and erudite author assures us of their authority. J. H. M., Jr.

A Text-book of Pathology. By Alfred Stengel, M.D., Sc.D., Professor of Medicine, University of Pennsylvania; Physician to the Pennsylvania and to the University Hospitals, and Herbert Fox, M.D., Director of the Pepper Laboratory of Clinical Medicine, University of Pennsylvania; Pathologist to the Philadelphia Zoölogical Garden. Sixth edition. Pp. 1045; 468 illustrations, with 15 colored plates. Philadelphia and London: W. B. Saunders Company.

Dr. Stengel's *Text-book on Pathology* was thoroughly and carefully revised in 1915 in coöperation with Dr. Herbert Fox. The present volume is a resetting of this sixth edition. In some ways this edition is comparable to the earlier previous ones, which have made the book a standard among pathological text-books. In many ways, however, extensive changes have been made, first in order to incorporate more of the pathological physiology, the study of

which has become so important to modern every-day medicine, and second to enlarge and extend the consideration of pathogenesis of diseases. In spite of these additions it would seem to the reviewer that even greater additions to these two sections would be of value. Pathology nowadays is concerned not only with the gross and microscopic changes that occur in the organs as a result of disease, but also takes into consideration the changes that occur as a result of the disturbance of functions that occur as a result of pathological changes. The value of the book would be greatly enhanced if such alterations in the physiology of pathological organs were enlarged and dealt with more extensively. J. H. M., Jr.

Diseases of the Stomach, Intestines and Pancreas. By Robert Coleman Kemp, M.D., Professor of Gastro-intestinal Diseases at the Fordham University Medical School; Gastro-enterologist at the Fordham University Clinic. Third edition, revised. Pp. 1096; 438 illustrations. Philadelphia and London: W. B. Saunders Company, 1917.

The third edition of this standard work appears enlarged and greatly improved in form. The book is extremely well written and absolutely complete in every way, and is one which the general practitioner may depend upon for a complete knowledge of a subject which is daily brought to him. The additions of this third edition include most notably a complete expedition of the roentgen ray as an aid to diagnosing particularly the organic defections of the stomach and intestines. Dr. Kemp has also incorporated the newer ideas in regard to protein infection, diverticulitis, and so on. It is a pleasure to commend the book. J. H. M., Jr.

Diagnosis and Treatment of Abnormalities of Myocardial Function. By T. Stuart Hart, A.M., M.D., Assistant Professor of Clinical Medicine in the College of Physicians and Surgeons, Columbia University. Pp. 320; 248 illustrations.

A growing importance of cardiac arrhythmias and the necessity of recognizing them when they appear is important. A book such as the present one written by Dr. Hart not only is of scientific importance, but a great clinical necessity. The various irregularities are considered fully and due prominence is given to those which are the most important. The book is to be thoroughly recommended and will prove extremely valuable to those who are interested and sufficiently scientific to wish to study carefully the various phases of cardiac pathology in its broader scope.

J. H. M., Jr.

A TREATISE ON DISEASES OF THE SKIN. By HENRY W. STELWAGON, M.D., Ph.D., Professor of Dermatology, Jefferson Medical College, Philadelphia. Eighth edition, thoroughly revised. Pp. 1309; 356 text illustrations and 33 full-page colored and half-tone plates. Philadelphia and London: W. B. Saunders Company.

IT is always a pleasure to review a volume which has the uniform excellence of Dr. Stelwagon's treatise. In reviewing the last five editions, in each, the author has accomplished his purpose of bringing the volume absolutely up to date. There is no cutaneous treatise that is more replete with reference, thereby giving the investigator, even if not a dermatologist, the opportunity for further study. The same high class of photographic art is exhibited, as in past editions; the new illustrations are uniformly good. The following diseases have either been added to the present volume or the sections dealing with the same revised: Occupational dermatose; paraffinonia; purpura annularis telangiectodes; xanthoma elasticum; ulerythema ophryogenes; pellagra; angioma serpiginosum; erythema elevatum diutinum; pemphigus neonatorum (impetigo contagiosa bullosa neonatorum), leprosy; the leukemias; eczematoid ringworm, and others.

Although there are many books published, a few of which excel the present volume in some detail or other, particularly the pathological aspect, there is none, however, all phases of the treatise considered, that surpasses the same. F. C. K.

FATS AND FATTY DEGENERATION. By MARTIN H. FISCHER, M.D., Eichberg Professor of Physiology in the University of Cincinnati, and MARTIN O. HOOKER, M.D., Instructor in Physiology in the University of Cincinnati. Pp. 155; 65 illustrations. New York: John Wiley & Sons, Inc., 1917.

THE book, or really monograph, is a collection and amplification of the results of experiments which have not ever before been published in English except in abstract form in *Science*. In the preface the authors say: "While our earlier colloid-chemical studies has compelled a desultory consideration of some of the problems here dealt with, this detailed study of the question of the fat in the cells is less than two years old. We turned to this fat problem in order to escape from older colloid-chemical studies on edema nephritis and allied subjects. Without intent on our part the conclusions of these newer studies dovetail with and corroborate the older ones. A house previously looked at from within is here seen from without—but it is the same house."

The novel scheme of giving an abstract of the entire monograph

in the first chapter is followed so that the busy man may get the gist of the subject matter. In this chapter, which is divided into ten parts to correspond with the ten chapters of the book, reference is made to specific pages in the book proper, so that elaboration on any particular point may be obtained with the least trouble.

The work should prove of interest alike to the chemist, biologist, and physician. H. E. D.

THE PHYSIOLOGY OF THE AMINO-ACIDS. By FRANK P. UNDERHILL, Ph.D., Professor of Pathological Chemistry, Yale University. Pp. 169; photograph and 12 charts. New Haven: Yale University Press, 1915.

IN preparing this book the author's aim has been "to gather together in one place the results which have thus far been obtained in the field of the biochemistry of the amino-acids, thus affording the busy practitioner, and others whose resources for consulting original communications are limited, an opportunity to gaining a knowledge of the present-day problems in this field of nutrition." For those who wish further information, references are given at the end of each chapter. An adequate knowledge of the fundamental principles of metabolism is presupposed as a preliminary to the proper understanding of the subject matter presented.

The derivation of amino-acids from proteins, the digestion, absorption, and excretion of the amino-acids, the theories of protein metabolism, the fate of the amino-acids and their relation to the specific dynamic action of proteins, the role of the amino-acids in nutrition and growth—all are dealt with briefly but concisely. The physician may complain that the book does not bear enough toward the clinical side, but it should be remembered that the attempt has been rather to indicate leading lines of thought to enable one to keep abreast of the times. It is to be hoped that the books of this form will continue to be written, so that the important findings of any one subject may be immediately available.

The book contains some misprints, the most glaring one being the formula for dextrose, which is given as $C_6H_6O_6$ twice on page 111 and twice on the following page. H. E. D.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO.

d-Glucose Tolerance in Health and Disease.—WILDER and SANSUM (*Arch. Int. Med.*, 1917, xix, 311) publish the results of investigations upon the tolerance of healthy and diseased individuals for glucose administered intravenously and at a constant rate. They used for the injection of the glucose solutions the apparatus described by Woodyatt and themselves (*Jour. Am. Med. Assn.*, 1915, lxv, 2067) which consists of a small pump driven by an electric motor, and so arranged that both the stroke of the pump and the number of strokes per minute may be increased or decreased at will. This permits of easy regulation of the rate of injection. They discuss the older methods of determining the sugar tolerance of animals, such as feeding experiments, subcutaneous injections, etc., and show that to accurately estimate tolerance, all factors which influence the rate at which the sugar enters the blood stream must be known. This is manifestly impossible to do when sugar is fed and absorbed through the alimentary tract, or when it is injected subcutaneously and absorbed from that locality. Therefore, if it is put directly into the blood stream at measured and carefully controlled rates, these errors immediately disappear. In order to have all conditions similar in the various experiments, the subjects for the tests were placed on a general mixed diet for several days preceding, none being given excessive amounts of carbohydrates. Only patients between twenty and forty-five years of age were used (one child of fourteen years), and the subjects remained at rest in bed on the day of the experiment, the injections being made between 2 and 4 P.M. No food was given by mouth on the day of the test, and in order that there should be no possible delay in glucose excretion once

the tolerance limit was passed, water was given by mouth during the day in such amounts that the subject received during each hour of the fore-period a quantity similar to that which he would receive during each hour of the test. A preparation of d-glucose of Merck was used at first, and later a high grade commercial glucose purified in the laboratory by decolorization with animal charcoal and repeated crystallization from alcohol. An 18 per cent. solution was finally fixed upon as the most satisfactory concentration for these experiments. The solutions were made with freshly distilled water, and in no test did the subject suffer any chill, shock or other general reaction. In 2 cases thrombosis of the vein used for the injection resulted, but in neither case was there any permanent ill effects. The injections are begun at a rate less than the estimated limit of tolerance and continued long enough to permit of thorough saturation of the tissues before the urine is collected and tested for sugar. This requires about twenty or thirty minutes. If the limit of tolerance has not been reached, the rate is increased, and in thirty minutes another specimen of urine is collected and tested for glucose. Two healthy men and two healthy women were used as the subjects in which to determine the normal limit of tolerance. This was found to be between 0.8 gm. and 0.9 gm. per kilo per hour. Three cases of pancreatic disease were tested and showed tolerance of 0.7 gm. per kilo per hour, 0.5 gm. per kilo per hour and 0.4 gm. per kilo per hour, respectively. Five patients with exophthalmic goitre were examined (2 men and 3 women), and in each case the tolerance limit for glucose was lowered; 2 severe cases showed a tolerance below 0.5 gm. per kilo per hour; two milder cases below 0.6 gm. per kilo per hour; and a still milder case had a tolerance limit between 0.6 and 0.7 gm. per kilo per hour. These findings are in harmony with the decreased tolerance shown by alimentary glycosuria in exophthalmic goitre patients observed by Kraus and Ludwig and others. A typical case of myxedema showed a normal tolerance, which is at variance with the results obtained in feeding experiments, in which an increased tolerance is found. A delay in the absorption rate is possibly the explanation of these results. Two cases of acromegaly, 1 case of suspected gigantism, and 2 cases of dyspituitarism showing Frölich's syndrome were tested, and all were found to have essentially normal tolerance limits. Here, again, the findings differ from those obtained on oral administration, and suggest that, as in myxedema, the increased alimentary tolerance must result from a delay in the rate of absorption from the bowel. One case of alcoholic cirrhosis gave a normal tolerance limit. The authors conclude that this method of determining the tolerance of patients for d-glucose is a practical clinical procedure, and is more accurate and gives more constant results than any other method which has been devised.

Septicemia due to Micrococcus Tetragenus.—Micrococcus tetragenus has largely been ignored as a pathogenic organism for man, but among the many other new medical facts which the war in Europe is eliciting are some interesting observations upon its pathogenicity which are reported by A. H. Birks, R. H. Thornby and R. A. Fawcus (*Quart. Jour. Med.*, 1916, x, 1, 37–38). The authors state that a large group of cases coming to the hospitals at the front in France are cases

which are clinically indistinguishable from paratyphoid fever, and in which none of the organisms of the typhoid group can be demonstrated. Professor Jacques Carles mentions three varieties of blood infection which produce these illnesses: (1) Micrococcus tetragenus, (2) pneumococcus, (3) Bacillus coli. The tetragenus infection is probably the most frequent, followed closely by the pneumococcal infections. These cases of obscure fever fall into two groups: The first resembles paratyphoid fever, and the second, in which the fever is intermittent, is called "trench fever." The authors believe that certain of the cases of these groups are infectious with Micrococcus tetragenus, and while not able to exclude absolutely this organism as a secondary invader following a primary paratyphoid, they believe this view to be highly improbable. In blood cultures from 100 consecutive cases of obscure pyrexia they isolated Micrococcus tetragenus in pure culture on twenty-five occasions, the cases of tetragenus infections possessing some rather characteristic features. It is apparently the weaker individuals who are most susceptible to the infection, and there seems to be some evidence that it is mildly infectious, as hospital orderlies are liable to contract it. The onset is usually sudden, though occasionally insidious, and the patient has headache, pain in the lumbar region and in the legs from the knees to the ankles. Tenderness over the tibiæ is common, and rather frequently an enlarged spleen and rose spots may appear. Anemia is common, and the patients are characteristically lethargic. The fever is of long duration (ten days or more in their reported cases), sometimes continued and sometimes remittent in character. The patients' serum agglutinates Micrococcus tetragenus, showing that the body has reacted to this organism. The authors had no fatal cases, so that no autopsy material was available, but they conclude that because of its frequency and its long duration it is of great military importance.

Results of Treatment of Hodgkin's Disease.—The generally accepted hopelessness of Hodgkin's disease, and its wholly unsatisfactory treatment are questioned by YATES and BUNTING (*Jour. Am. Med. Assn.*, 1917, lxviii, No. 10, 747). These authors discuss briefly the principles of treatment largely developed by them, and present the results of these methods applied in the treatment of 63 cases of the disease embracing all of its stages. They contend that treatment of the disease must be based upon the assumption that the pathological process involved partakes of the characters of a malign infection and of neoplastic growth, and they divide the cases into two groups, the first group consisting of the acute cases in which the disease runs its course to a fatal termination in a few months, and the second comprising the more chronic cases in which the end is reached in from two to five years. They also provide a scheme of classification for the chronic cases. The first principle which must be recognized in treating Hodgkin's disease is that, in the course of the illness, there are repeated and almost successful arrests of the morbid process, so that conclusions as to cures must be made only after a lapse of five years, during which time the patient has shown no evidence of the disease other than possibly a permanently subnormal lymphocyte count. The active treatment consists first in the elimination of possible portals of

entry for the infection (assuming that infection plays a part), such as inflamed tonsils, infected teeth and accessory sinuses, etc., followed by the radical extirpation of all involved lymphoid tissue that can be reached, that this infected tissue may not be a drain upon the patient's resources and further source of infection. This surgical intervention should be followed by thorough use of the roentgen ray, just as in removals of carcinomatous tissue. Immune sera, medication and general hygienic measures are also used to prevent extension of the disease. The authors state that wide surgical removal of the infected tissues, preceded by careful elimination of all possible portals of entry, and succeeded by careful and thorough use of the roentgen ray, can be successfully done with not more than 5 per cent. of local recurrences, or dissemination of the disease. They insist that the removal of tissue should be as complete as possible, and advise against "test excisions" except as a last resort in doubtful cases, where a frozen section diagnosis will be immediately followed by wide extirpation, or where the positive diagnosis will balance any danger to the patient which may result from possible dissemination of the disease. These excisions should be followed by the use of the roentgen ray. While not able to prove an etiological relationship of B. Hodgkini to the disease, the authors strongly advocate the use of an immune serum prepared with this organism because they have seen local reactions follow its use, with resulting diminution in the size of the glands, reduction in temperature and improvement of the subjective symptoms. Also they believe that patients who receive the serum and the general treatment do better than those who undergo the same general treatment without the serum. Arsenic they find to be of no lasting value, and they depend upon fresh air, sunshine and proper food, omitting all drugs other than tonics, which may be used if there is need for them. The results of these methods of treatment vary in the different groups of cases. The acute cases in the authors' words "are about as amenable to treat as is the mastitis carcinomatosa of lactation or melanoma." The incipient chronic cases in which only a few glands adjacent to an infected tonsil or other portal of entry are involved are exceedingly amenable to treatment consisting of the removal of the portal of entrance, roentgenotherapy and general hygienic measures. The diagnosis of these early cases is only made by careful physical examinations, routine blood counts and accurate interpretation of tuberculin tests. The authors estimate the possibility of recovery of the various groups of cases as follows: 5 acute cases, less than 5 per cent.; 5 incipient cases, 80 to 90 per cent.; 3 early cases, 60 to 70 per cent.; 11 moderately advanced cases, 30 to 40 per cent.; 14 advanced cases, 5 to 10 per cent.; 14 very late cases, palliation possible, 0 per cent.; 11 lethally involved cases, 0 per cent. The authors regret that as 67 per cent. of their patients presented themselves within the last two years they are unable to give more accurate figures as to ultimate recoveries. They believe that in 20 per cent. of all cases as seen by them recovery is possible, and they urge the importance of early diagnosis and the recognition of the fact that prompt and radical treatment may result in permanent recovery from Hodgkin's disease.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Principles of the Transfusion of Blood.—STANSFIELD (*Lancet*, i, 489) says that transfusion has been successfully employed in the treatment of various kinds of anemia and in the arrest of spontaneous hemorrhage. It has also yielded promising results in cases of serious infection and in certain toxemias. The ultimate prognosis in cases of anemia depends upon the power of reaction in the bone marrow, and this can only be adequately determined by observing the results of treatment. In cases of pernicious anemia both increased red-cell production and diminished red-cell destruction may result from the transfusion. The age of the patient, duration of the disease, and condition of the bone marrow as indicated in the peripheral blood have hitherto proved the best guides to the progress subsequent to the transfusion. The optimum dosage for transfusion is not yet determined, but it is probable that moderate repeated doses are preferable to large single doses in the treatment of chronic anemis. Very small doses may sometimes be of value. The donor should be a healthy adult with negative Wassermann reaction. The serum of the donor should not agglutinate the corpuscles of the patient, and the serum of the patient should not agglutinate the corpuscles of the donor. Agglutinins should be excluded by tests done immediately before the transfusion, and a single examination is not sufficient to establish the compatibility of the two bloods on all future occasions. If agglutinins are absent, hemolysins will also be absent. If there be great urgency and testing of the blood of the patient and donor be impracticable a small preliminary transfusion should be done half an hour before the main mass of blood is transfused, so that gross incompatibility may be recognized in time. Febrile reactions occur after about 25 per cent. of transfusions even though the bloods of donor and patient have been proved to be "compatible." Rigors occur in about 10 per cent. of the cases. It may prove desirable to investigate the blood of donor and patient with regard to factors of which we as yet know nothing, not merely for the sake of avoiding accidents, but also to determine whether a given donor is likely to afford the maximum of benefit in a particular case. The indirect method of transfusion, employing a glass received and sufficient sodium citrate to prevent coagulation of the transfused blood, is simple and involves no special dangers.

The Surgery of Amputation Stumps, Based on the Experience of 2000 Consecutive Cases.—HUGGINS (*Lancet*, 1917, i, 646) says that the surgery of amputations has entered a new era with the war. The old surgeons planned their operations essentially for speed and for the use

of peg limbs, and the classical operation for the foot belonged to an age when artificial joints had not been introduced. Primary amputations are performed to arrest infection and so to save life. Further operation, or radical treatment, is commonly necessary in England to prepare or improve, so that eventually a satisfactory limb may be fitted to it. The aim of this article is to elucidate this secondary treatment—that is, the preparation of stumps for artificial limbs. It is concluded that: No secondary amputations should be performed in cases of guillotine amputations until all edema has disappeared and skin extension has been employed for six weeks. Guillotine amputation stumps above the middle of the leg or thigh should never be shortened until healed unless it is decided that the knee-joint or hip must be sacrificed. When shortening has to be done the minimum amount of bone necessary for utilizing the joint above should always be borne in mind. A guillotine amputation may make a satisfactory stump in the leg and thigh, and almost always does in the forearm and arm without further reamputation. Bone in a stump does not necrose unless infected. Delay in shortening stumps reduces the risk of infection, because infection is not in the wound only but in lymphatics leading from the wound. The amount of matting round the vessels leading to or from an amputation stump is very striking. Silk should never be used in operations on stumps. Amputations should be done by skin-flaps only, and no muscle should be used in the flap, the pad of fibrous tissue formed over the end of the bone from the organizing clot being all that is necessary. All nerves, and not merely the main nerves, must be shortened at the time of the amputation or reamputation. To prevent deformity, daily exercising the joints and the employment of splints and bandages are essential measures in preparing the stump for the artificial limb. A good Syme amputation leaves the patient with little disability, and amputations through the tarsus should never be done as a secondary amputation.

Results of Local Anesthesia in Prostatectomy.—LEGEU (*Jour. d'Urolog.*, 1914–1915, vi (published in March, 1917), 601) reports his results with local anesthesia in 150 prostatectomies. He does the suprapublic operation and gives 0.01 centigram of morphin preliminary to the operation. He injects into the bladder 40 to 50 c.c. of the anesthetic solution, which is a 1 to 200 novocain solution to which a small quantity of adrenalin is added. No further anesthetization of the bladder wall is employed. When the bladder is opened two fingers of the left hand are introduced, facing the pubis, and they guide the special needles, long and bent into different angles. With these a series of injections of 5 or 6 c.c. of the solution are made around the adenoma, between the prostate and rectum, and anterior to the urethra. The eneucleation is then begun and is completed in about fifteen minutes. It has not been found necessary in any of his cases to give a general anesthetic. From 250 to 300 grams of the solution are employed, including the 40 grams injected into the bladder.

Scoliosis (Treatment).—ABBOTT (*Am. Jour. Orthop. Surg.*, 1917, xv, 244) summarizes the effective treatment of mild cases of scoliosis as follows: The posture of the deformity must be known. The normal physiological position from which it develops must be recognized, and

the principles of treatment—overcorrection and fixation—must be applied. The overcorrection consists of forcing the spine by the use of a corset into the normal scoliotic posture diametrically opposed to the deformity. The corset must be made from a plaster-of-Paris model, with the overcorrection position exaggerated. The corset must exert pressure at those points only when force is needed to bend the spine into the overcorrected position. The corset will do more harm than good unless accurately adjusted. The corset must be made with sufficient room for the patient to move over into the overcorrected position after treatment has been in operation for a time unless this is accomplished at once. The efficiency of the corset is to be determined only by taking skiagrams through it and by noting the position of the spine. Fixation in overcorrection must be continued until the structures are so changed that they are symmetrical. Unless a perfect balance or equilibrium of the spine is obtained the deformity is not completely reduced. In many cases the corset treatment must be supplemented by exercise, both active and passive, in order to obtain overcorrection. The exercise are given within the corset and with it removed. Exercises are given only in the direction of overcorrection, or in a direction that will not cause the body to assume the deformed position. After fixation has been maintained long enough to cause the necessary changes in the structures the overcorrection corset must be discarded. A straight corset may be of benefit for a time after the overcorrection corset has been discarded, in order to accustom the patient to the straight position. The after-treatment is important, and exercises which are symmetrical, together with massage, are indicated. The deformity must be attacked in the same manner as club-foot, and the same sound surgical principles of treatment that are so effective in reducing that deformity, must be applied, namely, overcorrection and fixation.

Pernicious Anemia, with Special Reference to Its Surgical Management.—PERCY (*Surg., Gynec. and Obst.*, 1917, xxiv, 533) says that we do not know why a given case will fare better without than with the spleen. Up to the present time no constant and typical pathology in the spleen has been observed. The changes found are such as could have been caused by an infective process, the effects of which are evidenced by fibrosis throughout and a moderate increase of lymphocytes. Phagocytosis of degenerated red cells is much more pronounced. The pulp areas are at times greatly crowded and dilated by red cells in various stages of degeneration. It would seem then that there is some process going on in the spleen which causes an increased destruction of red cells. While there can be very little doubt as to the theory of pernicious anemia being a hemolytic disease, it is not certain as to where or in what manner the hyperhemolysis takes place. A splenectomy, even in some of the late cases of pernicious anemia, has been followed by cessation of the hyperhemolysis, indicating that the spleen is at least an important link in the chain necessary for the production of the disease. While no surgeon can say that a cure has resulted from splenectomy or other surgical procedures in any case of pernicious anemia, still there is enough clinical evidence to show that the benefits derived from surgery are more than by any other means. Surgical treatment means more than merely splenectomy. The routine emphasized by Percy is:

Multiple, massive transfusions of whole blood, eradication of all local foci of infection present, laparotomy for removal of the spleen and other tissues showing evidence of chronic infection. Even though no ultimate cures may result, it seems that the work is worth while; that it offers at least the quickest and most certain method of obtaining a remission of the disease, even in some of the extreme and long standing cases.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

A Study of Ethylhydrocuprein (Optochin) in the Treatment of Acute Lobar Pneumonia.—MOORE and CHESNY (*Arch. Int. Med.*, 1917, xix, 611), in a comprehensive article, discuss the action of optochin as observed experimentally and also clinically. As judged from a series of 32 cases, when optochin hydrochloride was given by mouth to patients suffering from acute lobar pneumonia in such amounts that they received at least 0.024 gm. per kilogram of body weight per twenty-four hours, and when the size and spacing of the individual doses were adequately regulated, a specific pneumococcidal action appeared in their blood within a few hours, and could be maintained more or less constant for several days. In order to maintain the bactericidal action in the blood at a constant level, the intervals between the individual doses given by mouth should not ordinarily exceed about two and a half to three hours. When optochin is given by mouth according to such a scheme of dosage as outlined, the evidence points to some retention or accumulation in the blood of part of the drug absorbed. Administration of optochin hydrochloride by mouth appears to be more satisfactory than intramuscular administration. Further study of intramuscular administration appears to be desirable. Pneumococci not only *in vitro* but also in the human body in patients treated with optochin, may acquire the property of more or less complete resistance or "fastness" to the drug Toxic symptoms, such as tinnitus, deafness, amblyopia, or amaurosis (retinitis) may be observed in the use of the drug in man; they are generally transient. Retinitis, however, may result in more or less permanent impairment of vision.

The Effects of Salicylates on Experimental Arthritis in Rabbits.—FANTUS, SIMMONS and MOORE (*Arch. Int. Med.*, 1917, xix, 529) found that sodium salicylate, when used in a dose comparatively harmless to animal controls is decidedly detrimental and liable to be fatal to animals infected with the hemolytic streptococcus. The addition of sodium bicarbonate does not lessen much the harmfulness of the salicylate to infected rabbits. Sodium bicarbonate given alone is not

injurious to infected rabbits, neither does it produce a noticeable improvement. Acetylsalicylic acid in equivalent dosage appears to be much more toxic to normal rabbits than is sodium salicylate, and is harmful to infected rabbits as well. Salophene has either no influence or an unfavorable one on the course of the infection. The results of the experiments reported point to the conclusion that in the experimentally induced arthritis of rabbits salicylates are not only worthless, but even harmful. To bring these results in harmony with the clinically established usefulness of salicylates in rheumatic fever in human beings, several possibilities must be considered: (1) The Streptococcus hemolyticus used in these experiments might not have been the strain of streptococcus that is particularly susceptible to salicylate. It is well known that not all cases of infectious polyarthritis respond to salicylate in a specific manner; (2) it might be that there is a chemical difference between the system of the rabbit and that of man in its relation to salicylate; for example, a difference in the hydrogen (ion) concentration of the tissue fluids; (3) the action of salicylate in human beings might be merely symptomatic, but not really curative.

The Treatment of Tuberculosis with Cyanocuprol.—OTANI (*New York Med. Jour.*, 1917, cv, 537) says that cyanocuprol has been shown to be effective in cases of tuberculosis of varying degrees of severity. Of 22 patients that seemed to be hopeless and had been treated with all known methods, 8 showed marked improvement. The size of the dose seems to be closely related to the symptoms and the reactions. During the first period, when larger doses were employed, less beneficial results were obtained than during the second period when the size of the dose was considerably decreased. Cyanocuprol is effective in cases with fever, malnutrition, induration, and catarrhal condition of the lesion. In pulmonary tuberculosis the dull area and rales usually decrease, the number of bacilli in the sputum is diminished. The author has not yet studied a sufficient number of other forms of tuberculosis to permit any conclusions to be drawn. Injections of cyanocuprol sometimes causes general or lesional reactions in the patients. Febrile reactions were observed in 14.6 per cent. and lesional reactions in 25.6 per cent., based on the number of injections. These reactions were slight and transient. More severe reactions were produced in only 6.4 per cent. of the cases. During the first period in which the author had only a limited experience in the use of the drug, 7 cases showed unfavorable results; but during the second period there were none. The present communication is an additional contribution on this same subject, and the author now reports a total of 118 cases of tuberculosis treated on this plan during the past year.

The Nutritional Value of the Banana.—MYERS and ROSE (*Jour. Am. Med. Assn.*, 1917, lxviii, 1022) say that bananas have a higher caloric value than any of our other common fruits. Unlike most other fruits, they are always in season. When fully ripe, that is, when the starch has been almost completely changed to sugar, the experiments here reported show that the carbohydrates of the banana are well absorbed from the intestine. As sold in the market, however, bananas are frequently not sufficiently ripe to be consumed to advantage

immediately, and it would seem that gastro-intestinal disturbances when attributed to the banana were referable to this cause. It may be said, in general, regarding the experiments of the authors, that no ill effects, discomfort, or distaste were noted even after the consumption of large quantities of sugar (glucose, sucrose, levulose) may be given in the form of banana than as pure sugar (sucrose, glucose) without producing gastro-intestinal disturbances. The composition of the banana and the potato shows an interesting similarity both as regards total carbohydrate and the amounts of the different mineral constituents. While the banana can hardly be regarded as a potato substitute, the fact that it has practically the same caloric value as the potato is worthy of note. It is also of interest that both the banana and the potato yield an alkaline ash and are therefore antagonistic to the development of an acidosis. Of even greater importance is the fact that bananas may be eaten uncooked. This is of interest in view of the increasing significance that is being attached to the thermolabile "accessory food substances." The banana would appear to be a particularly valuable food to employ in the dietetic treatment of nephritic patients with nitrogen retention. Very satisfactory results have been obtained in the rather mild cases of nephritis here reported. As long as the patients exhibit no distaste for the fruit, there would seem to be no reason why bananas should not be employed in considerable quantity. The authors hope to report in the near future results obtained with this form of diet in cases of advanced nephritis.

Salvarsan and Neosalvarsan in Syphilis.—Ormsby (*Jour. Am. Med. Assn.*, 1917, lxviii, 949) is of the opinion that salvarsan and neosalvarsan are the most efficient drugs yet discovered in the treatment of syphilis. Alone they have completely eradicated the infection in early cases before the Wassermann reaction has become positive. The large number of reinfections testify to this fact. Yet even in these cases mercury is recommended as an adjunct. In all other cases, mercury should always be an accompaniment of salvarsan, and in many cases potassium iodide is indicated, especially in the so-called tertiary and latent cases and in those involving the nervous system. The ability of potassium iodide to remove infiltrations, gummas, and nodules, together with its marked effect on vascular implications, renders its use imperative. The major number of reactions following the use of salvarsan and neosalvarsan are insignificant. The more serious ones are to be avoided, so far as possible, by an initial small dose to test the tolerance of the patient, by careful attention to details in administrative technic, by recognizing contra-indications, and, in the case of early, active syphilis, preceding the salvarsan treatment with mercury, to prevent neurorecurrences; and finally by giving sufficient treatment to control the disease. The author lays emphasis on the latter statement, as much harm may be done by its apparent effect, the degree of relief placing the patient in a position of false security; therefore sufficient treatment is demanded to prevent recurrence and relapses. Many of the earlier cases, following insufficient treatment of rapid onset of symptoms which ordinarily come late in the disease, such as nervous involvement and precocious tertiary manifestations, were eradicated by more salvarsan, and now should be entirely

avoided by treatment of sufficient intensity and amount to control the disorder. The treatment of syphilis with salvarsan and neosalvarsan has caused an intensive study over the entire world of the question of efficient management of the disease, to such a degree that great lessons have been learned and much good accomplished. Their ultimate value will require many more years to determine as to a choice between the two drugs salvarsan and neosalvarsan, the extensive use of both proclaims their efficiency, so that individual circumstances with the physician and patient must decide which, under the circumstances, is to be selected. The apparent preponderance of opinion that salvarsan is more efficient is offset to a degree by the difficulties of its administration and the more frequent reactions following its use. Concerning the dangers following the individual injections, many warnings have been given to exercise care after the fourth injection. The warning has not been accompanied by tabulated results, showing proof of this contention. On the other hand, the statistics now available show that the major portion of severe reactions, untoward results and fatalities have followed the first injection, and that with subsequent injections these results were greatly decreased.

The Transfusion of Blood.—McClure and Dunn (*Bull. Johns Hopkins Hosp.*, 1917, xxviii, 99) give a brief summary of the history, various methods, necessary precautions and dangers of blood transfusion. They have given 150 transfusions to 80 patients and a tabulated summary of the cases so treated is included in the article. The authors have used transfusions in the following conditions: pernicious anemia, illuminating-gas poisoning, exophthalmic goitre, hemophilia, toxemia, shock, hemorrhage, leukemia, septicemia, purpura hemorrhagica, malnutrition, endocarditis, intoxication, general debility, dysentery, typhoid fever, infectious diseases, melena neonatorum, scarlet fever, pellagra, tuberculosis and tumors. It has also been used for vaccinating purposes. The best results have been obtained in hemophiliacs and babies with melena neonatorum; in the latter it is a specific, and in the former it stops the bleeding immediately, although without curing the disease. It is of great benefit in all anemias and with proper regulation may be of still more benefit in the primary types. Thus far, in shock it has been disappointing. This may be due to the fact that the shock has progressed too far before the transfusion has been done. They would advise a very early transfusion in cases of shock. Following acute and prolonged hemorrhage transfusion is of the greatest benefit. For gas poisoning, bleeding is beneficial, as was pointed out by Halsted. Depletion followed by injections of saline solution is as good, if not better, than transfusion. In tuberculosis there has been only slight benefit and so far, nothing has been accomplished by transfusion in malignant diseases in man. They believe that there is a great field to be developed in the line of vaccinating transfusions. Their experiences in typhoid fever have been very satisfactory. It would be very desirable to have a series of donors who have recently had typhoid fever ready to give blood to very ill typhoid patients. In one patient, depleted by hemorrhages as well as having a high-grade toxemia, the transfusion of blood, from a person who had previously had typhoid fever, brought about the most marked

improvement, the temperature dropping to normal and the hemorrhage ceasing, with a temporary disappearance of the toxemia. This is very suggestive of the good that might be accomplished by transfusing typhoid fever patients with blood from patients who have recently had the disease and who have probably a high grade of immunity. It would be interesting to try this type of transfusion in patients with other diseases and the procedure might prove very beneficial. A severe reaction occurred in 20 cases; a slight reaction in 25 cases; a chill in 15 cases; temperature elevation of over 101° F. in 34 cases; hemolysis in 8 cases. The results are summarized as life saving, 15 cases; beneficial, 63 cases; no benefit, 56 cases and harmful, 16 cases. Two deaths were probably due to transfusion, certainly one death was due to the improper matching of the blood.

The Passage of Neutralizing Substances from the Blood into the Cerebrospinal Fluid in Poliomyelitis.—Flexner and Amoss (*Jour. Exper. Med.*, 1917, xxv, 499) report that the cerebrospinal fluid taken very early and quite late in the course of acute poliomyelitis exhibits no neutralizing action on filtered poliomyelitic virus. The blood serum on the sixth day of the disease already contains the neutralizing principles. The injection of sterile horse serum into the cerebrospinal meninges in monkeys increases their permeability, so that they permit the immunity neutralizing principles passively injected with the blood to pass into the cerebrospinal fluid. The passage in passively immunized monkeys takes place during a relatively brief space of time and apparently only while the inflammatory reaction produced by the horse serum is at its height. It is established for monkeys and rendered probable for man that the intraspinal injection of immune serum in poliomyelitis is curative. In monkeys normal serum exerts no such action, and at present nothing can be stated definitely regarding the therapeutic effect of normal serum in man except that probably any benefits which may arise from its employment would be attributable not to the action of the serum as such, but to the escape of circulating immunity principles in the blood made possible by the aseptic inflammation set up by it in the meninges. As the immunity principles appear in the blood only after several days, and the reported favorable effects of the immune serum treatment relate to the first days of illness, the employment of normal serum is thus not indicated, while that of an immune serum is.

Lumbar Puncture for the Relief of Delirium in Lobar Pneumonia.—Musser and Hafford (*Jour. Am. Med. Assn.*, 1917, lxviii, 1231) report seven cases of pneumonia associated with severe delirium, in which relief of the delirium promptly followed lumbar puncture. The mortality rate was high, but as delirium is usually an indication of a severe infection, the authors feel that lumbar puncture offers a ready aid in controlling one of the symptoms which may so aggravate the patient's condition that what little chance he may have of surviving the infection would be lost were it not for this procedure. Lumbar puncture is, therefore, suggested as a measure to control a severe symptom, and not for any direct curative purposes.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Morphin-scopolamin during Labor. — GREENWOOD (*British Med. Jour.*, March 17, 1917) reports his experience in 150 cases of labor treated by morphin-scopolamin. But 2 cases failed to respond and showed no amnesia. These were patients in their own houses, multiparæ, who were not seen until labor was well advanced and in whom labor terminated very promptly. The writer thinks that it is vitally necessary that the physician be in constant attendance because morphin-scopolamin acts so variously upon different patients. There is no way of foretelling how many doses will be needed or how frequently. A routine method of treatment cannot be established. The time occupied in producing amnesia varies greatly and in these cases was from twenty minutes to four hours after the first injection. There were a number of abnormalities among the cases including three with mitral lesions and three with very marked albuminuria. These did well. There were 3 cases of postpartum hemorrhage in multiparæ who gave a history of having had this in previous labors. There was no maternal mortality among these patients and an infant mortality of 2 per cent., in which it could not be determined that the treatment had any influence upon the result. In 15 per cent. of the infants there was some interference with respiration. The study of the cases shows that to avoid interference with the infant's respiration morphin should not be given too late in labor or if it is necessary to use it, the dose should be progressively decreased. The best results are obtained when the treatment is begun early as soon as labor is definitely established. There seems to be no real delay in labor because of this treatment. The mother showed remarkable absence of exhaustion and shock. If this treatment is used to secure amnesia and not analgesia the writer believes that it has no danger for mother or infant. If pushed beyond this limit, the risk may be grave. To be used safely, the obstetrician must be constantly watchful during the labor. In over 50 per cent. of mothers the pulse-rate was considerably altered although the pulse showed no signs of weakness. The writer also states that among these patients were some who had positively refused to have a child because of the dread of physical suffering. By the use of this method, they were safely delivered without injury or pain.

Pyelitis in Pregnancy and Parturient Women.—GAMMELTOFT (*Ugesk. f. Laeger*, Copenhagen, January 18, 1917) has found in his experience that in its beginning pyelitis among pregnant women may simulate other intra-abdominal diseases. Cases run a very different course which also increases the obscurity of diagnosis. The colon bacillus is the cause of the disease in 70 per cent., and as pregnant women suffer habitually from constipation and often have disturbances

of the gastro-intestinal tract the occurrence of colon bacillus infection is readily explained. In its acute form the disease may declare itself quickly with general depression and fever and with or without a chill. It is common to observe nausea and vomiting in these cases. The patient may imagine that she is in the first stage of labor because the pains suggest labor pains. Usually after a time pain becomes localized in the kidney region, usually the right, occasionally in both. The ureter and bladder may be the seat of pain and tenderness. In the iliac fossa there may be considerable tenderness while at the symphysis there is very little or none. The urine is turbid and acid reaction. It has a putrid odor suggesting colon bacillus infection and albumin is sometimes present. On examination of the urinary sediment with the microscope usually a clinical diagnosis can be made without a bacteriological examination. In rare cases the urine is apparently normal because on the affected side the ureter has become blocked and only urine from a sound kidney is available for examination. The temperature fluctuates, often rising to 104–105. There are occasionally severe chills. The general condition usually remains good and the pulse is very little disturbed. If the case receives treatment, in about ten days the acute stage passes and the chronic follows. After the acute stage while the most significant symptoms of the disease may be lacking, the patient will complain of pain in the lumbar region and frequent desire for micturition. With these patients the urine should be examined thoroughly and if necessary cultures should be made. In pregnant patients it may be very difficult to ascertain exactly with what one is dealing. The pain and distress from which these patients suffer very closely resemble that cuased by appendicitis. Cystoscopy and catheterization of the ureters will often clear up the diagnosis. In treatment, rest in bed, moist heat over the painful area, and copious drinking of milk, lemonade, boiled water and weak tea are useful. Urotropin has given good results. In uring urotropin as much as 50 centigrams every four hours have been administered. Should there be retention of urine it may be necessary to catheterize the ureter at comparatively short intervals. It is best not to inject fluid into the kidney. Considerable help is seen in some cases by posture, turning the patient on the side opposite the infected kidney, when pressure upon the ureter will be relieved and the urine be discharged freely. Rinsing out the bladder is also useful and greatly relieves spasmodic pain. When the patient is convalescing, salol is often useful. An autogenous vaccine is thought to be valuable to prevent recurrence. The bacteria may be present in the urine for a long time after an attack and may change in their potency and development.

Cases of Apparent Appendicitis Complicating Pregnancy.—Van Trim (*Annal. de Gynec. de Obstet.*, 1916, xlii, 177) draws attention to the occurrence of symptoms in pregnant women precisely simulating those of acute appendicitis. In the first a gangrenous diverticulum was found at operation while the appendix was normal. In two other cases the symptoms were caused by suppurating dermoid ovarian cyst. The fourth patient had classic signs of sudden pain in the right lower abdomen but at operation the cecum and appendix were healthy. A collection of blood was found extending into the iliac fossa behind

and below the uterus and broad ligament. The case proved to be one of intra-uterine pregnancy and also ruptured tubal pregnancy. The fifth case was postpartum and the symptoms were caused by the twisted pedicle with partially suppurating ovarian cyst. It is not uncommon in parturient and puerperal women to have bilateral pain described in the lower abdomen. Occasionally this pain is unilateral and can often be traced directly to the region of the ovary. In some patients this pain follows nervous or psychic shock and is attended by no physical symptoms. In making a differential diagnosis the obstetrician should remember that young women may have an acute infective process with normal temperature and without rigidity of the abdomen, the cadinal symptom being high leukocytosis and the complaint of pain. This pain may occur periodically and may strongly simulate the pain of hysteria. Great help is obtained in diagnosis by the examination of the blood to determine the degree of leukocytosis present and the bacterial examination of the urine to determine the presence or abscess of colon bacillus infection of the kidney. Two cases in the experience of the reviewer illustrate this point. In the first, a young woman with a normal temperature was suffering from infection following a criminal abortion. She had no rigidity of the abdominal muscles and slightly subnormal temperature and rapid pulse. There was a foul discharge from the uterus. On admission to the hospital her condition was so grave that operation could not be performed. An autopsy rupture of the pyosalpinx and acute infection of the peritoneum were present. In a second case a young woman had produced upon herself abortion by inserting a slippery elm stick. She had a normal temperature, not much abdominal rigidity but complained periodically of severe abdominal pain. Her leukocytes were above 21,000. The pain was so pronounced and came so regularly that it seem hysterical in character. On section both Fallopian tubes exuded pus, the general peritoneum was injected, the appendix was normal. This patient did well with drainage of the pelvic cavity.

Morphin-hyoscin Method of Painless Childbirth.—HAULTAIN (*British Med. Jour.*, October 14, 1916) states that the method of Krönig and Gauss had not been accurately followed by the majority of the British obstetricians who have used the drugs. In the Royal Maternity Hospital in Edinburgh, Haultain and his staff rigidly adhered to Krönig's technic in the first 8 cases and the results were satisfactory. He observed that patients sometimes became restless and highly excitable and this seemed to be a personal peculiarity of the individual case. With some patients more than twenty-two injections were given during labor. Where it was impossible to obtain separate rooms for the isolation of the patient, the ward was darkened and screens placed about the patient's bed and cotton placed in the ears. Forty cases were so treated, 36 primiparæ and 4 miltiparæ. Smallest number of injections was four and the greatest forty-five. Usually $\frac{1}{4}$ grain morphin was given at the beginning with $\frac{1}{150}$ grain hyoscin. In 3 cases $\frac{1}{6}$ grain morphin was first used. In 3 cases morphin was repeated and the second dose was $\frac{1}{8}$ grain. In 30 out of 40 amnesia and analgesia were obtained. There was some effect in every case. In 3 cases the method failed. In 1 case there was marked restlessness

and injections had to be stopped. Postpartum hemorrhage occurred in 1 case and in 14 patients the forceps had to be applied. In 5 of these the instrument was used without chloroform and in the others chloroform was given. Of the 40 children, 5 were dead born, and of the 35 born living, 4 required artificial stimulation. In using the method in a primipara the first injection must not be given too early as it tends to stop the pains. When the os admits two fingers and pains are regular the drugs may be employed. In a multipara the injections can be begun as soon as labor starts. The second injection, $\frac{1}{150}$ gr. hyoscin should be given about one hour after the first injection and this can be repeated at intervals of one hour or three-quarters of an hour afterward. The morphin should not be repeated in the later part of the second stage because it tends to produce asphyxia in the child. The advice is given that if the hyŏscin is not taking effect, it is well to give the mother a slight whiff of chloroform. Thus the hyoscin is allowed to work and the patient passes into the condition of "twilight sleep;" 37 of the 40 patients got up out of bed on the third day after labor. We are somewhat interested to observe that the writer describes the administration of morphin hyoscin as the method of Krönig and Gauss. They employed scopolamin and laid great stress upon the absolute purity and quality of this drug. There is nothing new in the employment of hyoscin with nervous patients whether they be pregnant or not and morphin has long been known to be useful with nervous patients during labor. The suggestion to give chloroform to permit the hyoscin to take effect is an extraordinary method of treatment and one which does not appeal to us. We do not observe that the results of this treatment were specially satisfactory in avoiding the use of forceps, and yet it is supposed that if the patient be spared suffering her strength will be conserved and the use of forceps will be reduced to a minimum. After being extensively exploited by the public press and after a determined effort had been made to make the scopolamin method popular with the public, it has passed into the category of medical nostrums of doubtful value. The only benefit to the public and the profession which its attempted introduction produced was the study of the best and safest methods of lessening pain during labor and this brought out clearly that the scopolamin morphin method was difficult of application, uncertain in results frequently producing asphyxia in the child, lengthening labor and much inferior to other reliable and safe methods of treatment.

Joined Twins.—Iyer (*Indianapolis Med. Gaz.*, 1916, li, 237) reports the case of a woman who had been in labor three days. On examination a fetal head and left forearm had been delivered. A second head with its face turned toward the delivered one was also found. This could not be pushed up so was delivered with forceps without much difficulty. Both children were removed through the uterus and a common placenta was expressed shortly afterward. On examination it was found that the twins were attached by the cartilage of the ribs. There was a common abdomen covered only by peritoneum but there were separate pelvic bones and pelvic organs. There was one cord and one liver and spleen. There were two pairs of kidneys, a single heart, one diaphragm and two lungs.

The Combination of Morphin and Pituitrin in Labor.—Olivella and Arteaga (*Rev. med. de Sevilla*, 1916, lxvi, 1916) in 7 cases reported good results by using a combination of the hydrochlorate of morphine and extract of the fresh pituitary body and a sterile vehicle. Pain was greatly diminished, uterine contractions were better and the general condition of the patient remained good. Postpartum vomiting occurred in 1 case only and involution was normal. One child was born apneic but was readily revived. The children seemed stupid and breathed languidly during the first twenty-four hours after birth and required special care.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Surgical Traumatism as a Cause of Recurrence in Uterine Carcinoma.—Facts well known to every scientifically trained surgeon, but often not sufficiently kept in mind or acted upon, are well brought out in a paper by Shoemaker (*Am. Jour. Obst.*, 1917, lxxv, 758). He points out that it has been conclusively shown by Bloodgood, that in carcinoma of the breast the chance for recurrence is so increased by a preliminary excision of a specimen that permanent cure practically never occurs in cases where a piece of tissue has been excised for microscopic study and radical removal is not immediately carried out. Since it can be shown experimentally that tumor cells can enter vascular channels and be transported to a new radius of development, can anyone doubt the enormous importance of avoiding all squeezing of new growths accompanied by punctured wounds, such as occur in the use of double tenacula? No one would think of doing this with other malignant tumors, yet it has been customary with the uterus. The time required for any given blood corpuscle to circulate from the periphery to the heart and back to the periphery again has been estimated at from fifteen to twenty-three seconds. The time occupied between the start of a cell from a carcinoma, once entered the blood stream, to the heart and out to some peripheral point must therefore be calculated not in hours, not even in minutes, but in *seconds*, so that there is no time for operative excision to secure safety. For the time being, one may put aside the question as to what factor causes cancer; it is sufficient for this argument that where cancer cells are transferred in the blood stream they form under proper conditions a new nidus of the disease. The bearing of this upon the clinical study of a possibly malignant condition of the uterine cervix is obvious. In order to see, at times the temptation to use a tenaculum is very great. While inconvenient, however, a grasp may frequently be obtained outside the diseased area, and this should always be done, or the tissue grasped should first be cauterized. If unable to avoid making a preliminary microscopic

diagnosis (and this can be avoided in the large majority of cases), never excise a specimen except with the cautery knife, and for immediate diagnosis and immediate operation. Use no hooks! Obtain microscopic confirmation afterward if possible, but do not in the presence of clinical probability produce dissemination in a patient of cancerous age by surgical traumatism of an uncauterized growth.

Operation for Uterine Prolapse.—A novel and rather remarkable operation for the relief of bad cases of prolapse is described by HELMUTH (*Ann. Surg.*, 1917, lxv, 469). It consists in opening the abdomen by the usual vertical median incision, and then separating the adnexa and round ligaments from the uterus, as though a supravaginal hysterectomy were to be done without removing the tubes and ovaries. The uterine body is thus freed of all attachments down to the point of bladder reflection; the broad ligaments are whipped over exactly as after a hysterectomy, but the uterine body instead of then being cut away at the internal os is split sagitally from the fundus down to the level of the bladder attachment. The median incision in the fascia is now closed, and a short veirtcal slit, about a half inch in length, is made through the fascia and peritoneum on each side of the median incision, and parallel to it. Each half of the bisected uterus is now brought out through one of these slits, the fundus of the uterus being then sewed together again above the fascia, which thus runs through the uterine body between the cervix and fundus, keeping the latter permanently outside the fascial layer of the abdominal wall. The skin is then simply closed over the projecting uterine fundus in the usual manner. The author says that he has been able in this way to hold up permanently the prolapsed uterus better than by any other method he has used. If the cervix is large and hypertrophied, as is usually the case, it is amputated from below in the usual manner before opening the abdomen.

Hernia of the Bladder.—An unusual case of involvement of the bladder in an incarcerated femoral hernia has been reported by SALIBA (*Jour. Am. Med. Assn.*, 1917, lxviii, 1237). The patient, a woman, aged fifty-four years of age, was admitted to the hospital with a history of vomiting and obstipation with abdominal pain for four days. Examination showed a globular lump, the size of a small hen's egg, below and to the outside of the right pubic spine. It was hard, tense, tender, dull, and completely irreducible. On making an incision over it, and locating the sac, clear amber-colored fluid escaped as soon as the latter was injured. This was soon determined to be urine, and it was evident that the bladder formed part of the sac contents, and was adherent to it at the point of opening. The bladder injury was carefully closed, and dissected free from the sac wall. There was also a loop of intestine in the hernia, the strangulating agent in which was found to be not Hey's ligament, but the mouth of the sac itself, which was found to be greatly thickened. In dividing this thickening the bladder was again accidentally wounded, and was again sutured, after cleansing the wound with ether. The operation then proceeded in the usual manner, and has resulted in permanent relief of the hernia. No drainage was used.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Concerning Renal Sclerosis.—What at one time appeared a very happy agreement between several authors on Bright's disease (Jores, Loehlein, Fahr) has now resulted in confusion wherein each of these men stands by himself for a separate theory of the disease. Jores can see but one factor underlying the development of renal sclerosis and that is arteriosclerosis. To him the tissues of the kidney other than the arteries appear to play only a passive role and give evidence of morphological and functional disturbance in proportion to the arterial lesion and its effects upon the circulation. He gives no clear view in what manner the development of the benign fibrosis of the kidney differs from that of the malignant. Loehlein broadly agrees with the views of Jores. He recognizes the two types of renal sclerosis, but appears to regard the malignant one as nothing else than an advanced stage of the benign. He takes it that it is only a matter of the extent of the involvement rather than a difference in kind. For the determination of the injury resulting in the kidney from these arterial lesions attention is particularly attracted to the glomerular changes and the degeneration of the tubules. FAHR (*Cent. f. Path.*, 1916, xxvii, 481), on the other hand, although considering the vascular lesion as essential and primary, believes that another factor must be superimposed for the production of malignant fibrosis of the kidney. As to the nature of this added factor he has little to offer definitely. This type of kidney disease with a dual etiological factor he prefers to speak of as the "combination type." His descriptions of the actual changes occurring within the kidney are very similar to those long ago described by Gull and Sutton. None of the authors appear to be familiar with the early work of Councilman, and although all of them recognize the common arterial lesions in interstitial nephritis they appear to lay no stress in their studies upon the causes of these processes. It would appear that no useful purpose is to be attained through the polemic by these authors as long as they make the subject of their controversy a late incident in this important disease.

Diminution of the Number of Islands of Langerhans in Diabetes.—Various authors have claimed that there is a definite diminution in the number of islands of Langerhans in diabetes. In 1900 Ssobolew

claimed to have observed the complete absence of island structures in 2 cases, while later he found 4 others with a similar condition. In 9 he noted a definite diminution in the number of islands but as he did not study portions of tissue from different parts of the pancreas, it is impossible to lay much stress on his observations. Subsequently Weichselbaum observed the unequal distribution of the islands in the pancreas in normal individuals and found that these structures are always more common in the tail than in other parts. Similar observations were made by Opie and Cecil. Martius examined a series of 27 cases of diabetes and was unable to support the contention that there was any relationship between the number of islands found and the occurrence of glycosuria. In these analyses portions were obtained from various parts of the pancreas and an estimate of the number of islands was made in a constant area of 0.5 square centimeter. Although the number of islands in a few cases was less than normal, it was claimed that a larger proportion of cases of diabetes showed no comparable change. Martius laid more stress upon the presence of morphological changes in the islands than upon an actual diminution in the number. Recently HEIBERG (*Cent. f. Path.*, 1916, xxvii, 49, and *Arch. f. Kinderheilkunde*, 1916, lxv, 388) carried out similar studies upon the relationship between the numbers of islands and diabetes. He divided the cases of diabetes into two groups: (1) Those showing pathological changes in the islands only; (2) those with wider involvement. It is the first group which particularly attracts attention and of which it is so commonly stated that true clinical diabetes was present without definite pancreatic lesions. In this group, it is found that a certain number of cases show definite island lesions which although not involving all of these secreting structures, materially interferes with function. When hyalin and other degenerations are observed the diagnosis of the pancreatic affection is not difficult. But in those cases where the island lesion has led to the disappearance of many of them and where the remaining ones appear normal or even hypertrophied, it is difficult to point to the damage in the pancreas as associated with diabetes unless a numerical diminution in the number of these structures can be determined. In an analysis of 12 of his own cases along with a group of others taken from the literature he claims to have established definite evidence showing a decrease in the number of islands. These analyses were made by careful counts in sections taken from various portions of the pancreas. When compared with observations upon the normal pancreas it is shown that this diminution is fairly constant. The author also reëstablishes the tables compiled by Martius and shows that this author obtained the same results. Heiberg, furthermore, finds that a similar diminution in the number of islands may be demonstrated in the pancreas of children ill with diabetes.

Studies of the Betahemolytic Streptococci.—The relation between scarlet fever, streptococci and septic sore throat is a subject which has always been very puzzling to investigators. Septic sore throat has been proved by many observers to be due to a type of streptococcus named by Smith and Brown, β-hemolytic streptococcus. Scarlet fever although so commonly associated with streptococci has not been

proved to have any direct relationship to this organism. SMILLIE (*Jour. Infect. Dis.*, 1917, xx, 45) reports a study of three epidemics of septic sore throat, in some of which the relation between scarlet fever and this condition is very suggestive. One epidemic occurred in the town of Dorchester among customers of a certain dairy. Although three farms supplied milk to this dairy and sources of β-hemolytic streptococci were found in each, one employee of one of the farms had a history suggestive of an attack of scarlet fever just previous to the outbreak of the epidemic. The second epidemic was in a boys' boarding school where 17 cases of septic sore throat occurred. The milk used by all these boys was found to have been insufficiently pasteurized, and the examination of the cows from which the milk was obtained showed the presence of this type of streptococcus in one of them. No cases of scarlet fever were found in this outbreak. The third epidemic occurred in a hospital and was proved to be a combination of milk-borne and contact infection. Another interesting group of cases was also found by this observer. Three small girls who played together on a Monday afternoon, all became ill on Thursday of the same week. One developed a typical case of scarlet fever. The second a very mild case of the same disease, while the third developed a very severe septic sore throat but showed no skin rash nor any other sign of scarlet fever. β-hemolytic streptococci were found in the throats of all three girls. In careful bacteriological studies of all of these cases both during the disease and convalescence and also in studies of normal throats, the author found β-hemolytic streptococci so frequently that their importance in septic sore throat appears established and in scarlet fever is a matter not to be considered too lightly. The organism is one which grows in variously sized chains, shows some capsular substance and on blood-agar causes a very wide hemolysis around each colony, this zone sometimes being 5 mm. wide. The carbohydrate reactions as given in this paper are not particularly valuable. Cultures on carbohydrate medium were titrated for quantity of acid and this has been proved by Broadhurst, and also by Holman to be a method, the results of which vary with many factors such as medium, vigor of growth, etc. From the results of the carbohydrate fermentation given by the author this streptococcus would come under the head of Streptococcus infrequens in the classification of Holman. This streptococcus has been found by a number of other observers in the throats of scarlet fever patients and has been easily recognized by them by means of its hemolysis and also by its characteristic carbohydrate reaction. The fact that it is not a frequent inhabitant of normal throats and occurs almost always in the above mentioned conditions is, as the author states, very suggestive of the relationship between these two diseases and the danger to a community of the presence of either of them.

Observations on the Mode of Origin of the Fibro-adenoma of the Mammary Gland in the Rat and on the Delayed Retrogression of the Mammary Gland after the Period of Lactation.—In the report of a study of four curious neoplasms in the breasts of a female rat, LOEB (*Jour. Cancer Research* 1916, i, 415) offers some interesting suggestions on the mode of origin of fibro-adenomata in these animals, and

on the condition resulting from delayed retrogression of the mammary gland following lactation. Admirable microscopic descriptions of the tumors are given. One resembled, in the gross, an ordinary fibro-adenoma. In sections, however, the character was that of a recently functionating mammary gland, within some areas vacuolated cells in acinar arrangement and a well-developed stroma. In a few places there was a relative increase in epithelial elements, as though the stroma had been reduced in amount. The author concludes that the failure of normal retrogression is the cause of fibro-adenomata in the breast of the rat. In this connection he gives no hint that growth of fibrous tissue had occurred, nor that epithelial elements had proliferated. Nor is there any indication that the growth was encapsulated, but rather one is led to infer that the whole breast is considered a tumor. This entails a special classification of tumors for the rat. The writer invokes a special local condition of unnamed sort to account for the reaction in this breast, but rules out infectious processes. Here is drawn an unfortunate parallel between the subinvolved breast and hepatic cirrhosis. The writer establishes simultaneous development of connective tissue and epithelial elements as the picture in cirrhosis of the liver though in the next paragraph one finds him agreeing with Weigert in the view that "hypertrophic proliferation of connective tissue is invariably the result of primary destruction of epithelium," a contrary notion to that of Mallory that pure parenchymatous degeneration rarely stimulates fibrosis, which occurs only when the stroma has also been affected by the irritant. In view of these facts, one hesitates to so readily relinquish the factor of a local irritant, even possibly a bacterial one. The other three mammary glands proved to be enlarged due to a cystic degeneration of the breast tissue. All were of the nature of single large cysts, containing a thick yellow fluid, possibly autolyzed material. Microscopically, the cysts were lined by a low cuboidal epithelium, interrupted in places by areas where necrotic tissue was adherent over a base of granulation tissue. In the cyst wall are compressed epithelial acini, some of which are cystic. Many small cysts frequently are jointed to the larger cavity, with the result that papillomatous masses covered by epithelium, project into the larger cavity. The statement is made that the necrosing masses adherent to the cyst are cut off from the healthy tissue by the growth of the lining epithelium through such masses at the pedicle. As a cause for this degenerative process and necrosis some "general factor, delaying the normal retrogression of several glands" seems less inviting than the comparison barely mentioned by the writer between this process and the casting off of the normal placenta. The effect of an obliterative endarteritis, in cutting off nutrition, might well be considered. And there is no reason to suppose that this process could not go on in different glands at the same time.

A Study of Experimental Non-hemolytic Streptococcus Lesions in Vitally Stained Rabbits.—Cecil (*Jour. Exper. Med.*, 1916, xxiv, 739) records experiments on rabbits in which he injected both Streptococcus viridans and trypan-blue. The doses were various and were given at intervals. The lesions which he obtained were striking and it is to be regretted that he did not classify any of the streptococci used but included them all under the heading of that very large group known

as non-hemolytic streptococci. Three of his strains were obtained from cases of rheumatic fever and three from cases of infectious endocarditis. The trypan-blue staining was of great assistance in studying the lesions, particularly in regard to the source and fate of certain inflammatory cells which were found in the lesions. The lesions noted were joint lesions which began as mild exudative inflammations and progressed to very severe types with fibrosis and in some cases destruction of cartilages of the joints and also some destruction of the underlying bone. The lesions in all cases were similar to those found in the human under the same circumstances. Heart lesions, both pericardial and endocardial, were rather infrequent and irregular but myocardial lesions were common though not similar to those described by former observers. Liver and kidney lesions occurred occasionally but were not characteristic and could not be compared with the lesions in the human. The value of the use of vital staining in the study of inflammatory cells particularly in relation to the source of these cells is demonstrated in this work. The injection of vital stains, however, changes to some extent the cell picture of inflammations and the author notes that this point should not be overlooked in such studies.

A Contribution to the Epidemiology of Lobar Pneumonia.—SILLMANN (*Jour. Exper. Med.*, 1916, xxiv, 651) sums the findings of mouth, lung and blood cultures of pneumonia patients and also mouth cultures of normal individuals taken at the Hospital of the Rockefeller Institute during four years. The cultures were taken from patients during the disease and for various periods after recovery in an attempt to note the incidence of carriers in convalescent patients and also to note the average length of time after recovery that the virulent pneumococcus remained in the mouth. Although the incidence of the Types I, II and III, and III vary somewhat from year to year, I and II are always the most frequent types. Type IV does not vary greatly and is next in frequency. Type III gives the smallest percentage of cases in most reports. Types I, II and III remain in the mouth for varying lengths of time after recovery from disease produced by one of them as does also Type IV. Type IV is very frequently found in the mouths of normal individuals whereas the other three types are not so frequent under these circumstances. In the case of III which is the most virulent pneumococcus and which occurs in the fewest number of cases of pneumonia, the incidence in normal mouths is relatively large and Types I and II are quite infrequent. All the cases listed under "normal mouths" are, of course, cases which were not in contact with pneumonia patients. In the mouths of nurses, doctors and relatives of pneumonia patients who are in fairly intimate contact with the case, a type of pneumococcus is frequently found which corresponds to the type isolated from the patient's mouth or lung. It is in these individuals that Types I and II are found most frequently because they are the most frequent organism found in patients. As to carriers it was found that IV was widespread. Type III is not very frequent and Types I and II did occasionally occur in mouths of individuals in whom it was impossible to trace any instance of contact. From these figures it is evident that even though chronic carriers of the virulent types of pneumococci are rather infrequent the danger from contact carriers is not to be ignored.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON; MASSACHUSETTS,

AND

JOHN F. ANDERSON, M.D.,

FORMERLY DIRECTOR OF THE HYGIENIC LABORATORY, PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Studies of the β-hemolytic Streptococcus.—SMILLIE (*Jour. Inf. Dis.*, 1917, xx, 45) states that the β-hemolytic streptococcus was found by Theobald Smith and J. Howard Brown to be the etiological agent in several milk-borne epidemics of septic sore throat. They believed the strain to be a human type, though it may be introduced into a cow's udder and produce a mild reaction. It has definite characteristics which distinguish it, and which have been described by Smith and Brown. Smillie repeated the work of these authors in the study of the epidemiology of two outbreaks of milk-borne septic sore throat. In each epidemic, the β-hemolytic streptococcus was found in the throats of the victims. In one epidemic, the same strain of streptococcus was found in the suspected milk. In the other epidemic, the β-hemolytic streptococcus was isolated from a mildly inflamed udder of one of the dairy cows. In order to ascertain the prevalence of the β-hemolytic streptococcus in normal throats, 100 average throats were searched for the types of streptococci present, and though many hemolytic streptococci were found, the β-hemolytic type of streptococcus of Smith and Brown was found but once. The throats of 20 individuals who had had milk-borne epidemic septic sore throat within two years were searched for the β-hemolytic streptococcus in order to estimate the prevalence of carriers of this strain. One carrier was found, a nurse who had had septic sore throat four months before. This nurse had later been the cause of a small contact infection epidemic of tonsillitis, thus illustrating the relation between the sporadic and epidemic mode of infection. The throats of 20 cases of sporadic tonsillitis were studied in order to ascertain the proportion of cases of ordinary tonsillitis due to the Smith streptococcus. Five of the 20 cases were found to be due to the β-hemolytic type of streptococcus. Finally, the prevalence of the β-hemolytic streptococcus was studied in 48 cases of scarlet fever. This strain was found in the throats of all the severe cases, and in some of the moderate and mild cases of the disease. There seemed to be a close relation between the severity of the disease, and the numbers and virulence of the β-hemolytic streptococci in the patients' throats. The same type of streptococci were also found in the aural and nasal discharges of four suspected carriers of scarlet fever. In all these diseases—septic sore throat, sporadic tonsillitis and scarlet fever—the β-hemolytic streptococcus was found in gradually diminishing numbers throughout con-

valescence, usually disappearing from the throat in ten to fourteen days. The author believes that epidemic tonsillitis, or septic sore throat, is not wholly due to the use of contaminated milk, but that it may be spread by direct contact. The β-hemolytic streptococcus is rarely found in normal human throats, and carriers are not common. Thus, though the flora from human throats frequently finds its way to the daily milk supply, milk-borne epidemics are not of daily occurrence. The great menace to the community is the convalescent case of septic sore throat, sporadic tonsillitis or scarlet fever, for this individual is a source of danger, insofar as he comes in intimate relations with his fellows; spreading disease to the individual by direct contact, or to the whole community by infecting the milk supply.

The Influence of Milk and Carbohydrate Feeding on the Character of the Intestinal Flora. Diet versus Bacterial Implantation.—HULL and RETTGER (*Jour. Bact.*, 1917, ii, 47–71) remark that the culmination of several years of investigation carried on in the Sheffield Scientific School of Yale University corroborates the earlier experiments on animal feeding in which the following points were definitely determined. A change in the diet of white rats from the ordinary mixed food to one containing starch, lard, protein-free milk and a pure protein quickly led to a simplification of the intestinal flora, the Gram-positive organisms being displaced by Gram-negatives. B. coli was practically eliminated, while members of the B. acidophilus predominated or constituted almost the entire flora. Milk and lactose were particularly effective in establishing the acidophilus group. In milk feeding B. acidophilus became abundant, while in continued lactose feeding it was usually supplanted by B. bifidus. Carbohydrates other than milk-sugar fail to bring about this transformation. The ingestion of foreign bacteria, even in large numbers, did not of itself bring about an elimination of the common intestinal microörganisms. The feeding of B. bulgaricus tablets without the use of milk or lactose can, therefore, be of little or no value. In the present investigation the following additional facts were obtained. Meat or other high protein diet increases the indol-producing bacteria and other organisms of the so-called "putrefactive" type, like B. coli and B. welchii; cornstarch appears to foster the amylolytic group of intestinal organisms, while in a few instances grain feed favored the development of what appeared to be fusiform bacilli. The reaction of the intestine remained independent of the character of the intestinal flora. While the acidity varied in the different rats, it was not increased during the lactose feeding. When lactose was given in dry form its presence could be detected in different parts of the intestine; during the feeding of lactose in solution the identification of the sugar in the intestine was much more difficult. The rapid development of the aciduric bacteria when a lactose diet is given in all probability is due to optimum cultural and environmental conditions which are created for these particular organisms by the lactose, although it may be present in very small amounts. A high lactose diet markedly influences the intestinal flora of man, though relatively large amounts of this sugar are necessary to bring about extensive changes in the flora. These facts have been amply corroborated by the work of other investigators. One

of the most important points established in the present work is the inability of a foreign organism to establish itself in the intestine of man or animal, except in disease by mere intestinal implantation.

The Clarification of Milk.—HASTINGS (*Jour. Am. Med. Assn.*, March 24, 1917, p. 899) states that careful experiments show that the bacterial content of milk is apparently increased by clarification, due to the breaking up of clumps. Clarification has no favorable effect on the keeping quality, and probably does not in any way improve the milk. It removes the dirt, but not the bacteria, pathogenic and otherwise, which were introduced with the dirt. It is hard to understand why health officials sanction clarification, yet the cities of St. Louis and Cincinnati, Ohio, Gary, Indiana, and Tulsa, Oklahoma, have passed ordinances requiring clarification, supposedly with the approval of the respective health departments. The introduction of pasteurization is opposed to by health officials because it enables the dealer to handle a poorer grade of milk than he otherwise could. Although this is, perfectly true, pasteurization gives the consumer a product more safe and of better keeping quality than the raw product. The clarification of milk is objectionable from the stand-point of the consumer, and yet health officials are apparently being led to urge its adoption.

Is Mosquito or Man the Winter Carrier of Malaria Organisms?—MITZMAIN and BRUIN (*Public Health Bulletin* No. 84, December, 1916, U. S. Public Health Service) studied the problem of quinin sterilization of the human host of malaria during the winter period; specially to determine: (1) If man alone harbors malaria parasites during this period. (2) If the mosquito is a potential factor in the perpetuation of malaria from fall to spring. The bulletin is an outcome of an intensive study conducted to determine for one locality at least, the relation of man and mosquito as influenced by the dormant conditions existing in the winter months in the southern United States. A group of fifteen plantations in the Mississippi Delta of the Yazo valley, having a known malarial index of over 40 per cent. comprised the district in which the investigation was conducted. At the outset, it was required to ascertain in what stage of its life history Anopheles mosquitoes existed. It was noted that for this region only intermittent hibernation prevailed and that the adult female mosquito was the only form observed to hibernate. It was ascertained during the course of the winter studies that in this region occasional biting of aroused Anopheles did not have any pathogenic significance, all of the infections clinically noted were proved to be recurrences of former attacks. It was concluded that hibernating anophelines collected in the region investigated, did not harbor parasites of malaria. This was determined after an examination of 2122 dissected anophelines, of which 1211 specimens were examined before May 15, 1915. Among the remaining 911 specimens, serving as a malaria indicator for the spring season, 3 mosquitoes between May 15 and May 26, were definitely shown to contain oocysts indistinguishable from those seen in mosquitoes experimentally infected with human malaria. In the investigation of man as the responsible winter carrier, 1184 persons, residing on the plantations selected, were examined for malaria parasites.

Four hundred and ninety-two infections were identified microscopically, 317 cases were of the subtertian type, 8 were mixed infections, and the remainder were of the simple tertian type, with the exception of one quart case. In the consideration of these infections an important fact stands out: nearly one-fourth (24.8 per cent.) of the human carriers harbored gametocytes. It was proved that from a group of 103 persons, examined in March, 1915, 8 of the 15 gametocyte carriers identified, were similarly infected during the preceding fall. The incrimination of man as the sole winter carrier is emphasized by the fact that 3 malaria infected Anopheles quadrimaculatus were found in the homes of the gametocyte carriers during May 15 to May 26, previous to which time 1180 specimens of anopheles from this source were found to be negative.

Laundries and the Public Health.—SCHROEDER and SOUTHERLAND (*Public Health Reports*, February 19, 1917, xxii, No. 6) state that the purpose of this study is to ascertain the methods employed in New York City laundries with special inquiry into the efficacy of such methods in destroying pathogenic bacteria and thus preventing the spread of disease. The survey includes the following: (1) Methods employed in handling clothes in the home. (2) Methods employed in handling clothes in the homes of laundresses. (3) Methods employed in handling clothes in the hand laundries (white and Chinese). (4) Methods employed in handling clothes in the steam laundries. (5) Series of special tests of goods to note the effect of heat upon bacterial life. (6) A canvass of steam laundry managers to ascertain their opinions concerning the use of nets in laundries. The authors found the methods of dealing with laundry in the home to be quite sufficient to make the danger from infected linen negligible. The laundry which is done in the home of a laundress is usually clean and free from bacteria; but owing to the close quarters in which tbe laundresses live, there is a possibility of reinfection of clean linen if communicable diseases are present among the members of the laundress' family. Of the so-called hand laundries, of which there are 2800 in New York City, there are three groups: (1) Laundries known as feeders for the steam laundries and maintained by them for sorting, marking or distributing. (2) Laundries operated by private individuals who do some washing and practically all the drying and ironing on the premises. (3) Laundries operated by private individuals practically doing on the premises all the washing and ironing for patrons. This group includes all the Chinese laundries. After a careful study of the location of and conditions in these laundries, the methods of sorting, washing, drying and ironing the clothes, the authors make the statement that the so-called "hand laundries" are, to some extent, a menace to the public health because of the crowded living quarters connected with the laundries; because of the probability of infectious diseases occurring among the persons living in such quarters without proper means of isolation; because of the careless method employed for sorting the clothes, allowing the contact of clean and soiled linen; because of the packing of nets with a heterogeneous mass of clothes which cannot be penetrated by the proper amount of wash water, and to which cannot be applied the proper degree of heat nor amount of disinfectants; and because of the

lack of proper facilities for drying and sorting the clothes, and the general insanitary conditions under which the work is carried on. The conditions in the Chinese laundries were, on the whole, better than those found in the laundries maintained by white people. In the investigation of the steam laundries, the methods were as follows: Bacteriological tests were made of: (1) The bactericidal strength of water plus the soap and disinfecting solutions and the possible mechanical elimination of large numbers of bacteria in the process of washing. (2) The penetrative power of the heat employed in washing. (3) The value of the ironing processes in the destruction of bacteria. (4) The value of the drying processes. Of the steam laundries in New York City there are several groups: (1) Laundries connected with infectious disease hospitals. (2) Laundries which deal directly with families or individual patrons, and in which the clothes are washed and finished. (3) Laundries dealing indirectly with families or individual patrons through the medium of hand laundries. (4) Wet-wash laundries. The methods employed in laundries connected with infectious disease hospitals are described separately and a review of these leads conclusively to the belief that pathogenic organisms are destroyed by these methods. From a study of the other groups included under the steam laundries the following conclusions were reached: The comparatively few steam laundries which use standard routine methods of washing and keep a record of the time, material and solutions employed are getting better results than the average establishments. The methods employed by steam laundries in the collection and delivery of clothes are insanitary—soiled and clean clothes being brought into close proximity. In the majority of laundries clothes are washed under conditions prejudicial to the health of the employees. The method, quite commonly employed, of returning "wet" clothes to the patrons and to hand laundries is a possible menace to the public health. Wet clothes infected with bacteria and subjected to the usual degree of heat in drying houses, "tumblers," mangles and hot presses are freed from living organisms. The practice of wet washing, as now done in steam laundries is insanitary as the clothes do not receive the proper application of disinfectants, soap, water and heat. Owing to the difficulty of ascertaining whether clothes have been properly heated during the washing processes, and the possibility of the transmission of infection when not properly heated, all clothes washed in steam laundries should be dried upon the premises. The absence in the average steam laundry of proper sorting rooms for the clean linen and the consequent contact with soiled linen may result in a possible reinfection of the clean clothes.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this* JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

Parathyroids—
Powder and Tablets. 1-30 grain.

Red Bone Marrow—
(Medullary Glycerides) Hematogenetic. Hemogenetic.

Corpus Luteum— (Free Substance)
Powder, Tablets and 2 and 5 grain Capsules

Armour's LABORATORY PRODUCTS

Elixir of Enzymes—
Digestant and palatable vehicle.

Pineal Substance—
Powder and Tablets. 1-30 grain.

Pituitary, Anterior—
Powder and Tablets. 2 grain.

Pituitary, Posterior—
Powder and Tablets, 1-10 grain.

Pituitary Liquid

(*Armour*)

A pure, potent preparation of the Posterior Pituitary Body. Uniform and reliable alike, in surgical and obstetrical work.

PITUITARY LIQUID *(Armour)* is entirely free from local anesthetics and other objectionable preservatives.*

PITUITARY LIQUID *(Armour)* standard strength, is supplied in two sized ampoules, 1cc and ½cc, 6 in a box.

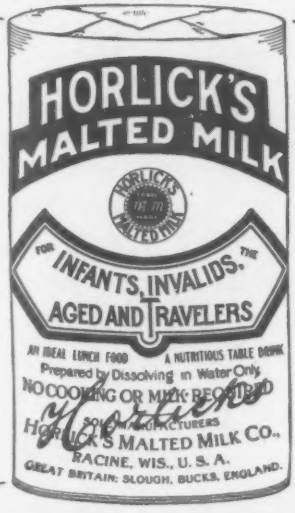
* Vide Hygienic Laboratory Bulletin No. 109.

ARMOUR & COMPANY
CHICAGO

1499

Horlick's the Original Malted Milk

This is the package. Others are substitutes.



Palatable, agreeable and beneficial to infant, invalid and convalescent.

Horlick's Malted Milk Company, Racine, Wisconsin

We invite comparison

When you administer a hypodermatic tablet solution you want prompt action. You want a definite therapeutic result.

If you use a tablet of our manufacture you have assurance that both objects will be achieved.

HYPODERMATIC TABLETS

P. D. & Co.

are prepared from rigidly tested materials—materials that are guaranteed as to identity, purity and potency.

Hypodermatic Tablets, P. D. & Co., insure definite dosage. The content of each tablet is accurately determined. The medicament is uniformly subdivided by an unerring mechanical process, giving assurance that the active component is present in the precise amount indicated by the label.

Hypodermatic Tablets, P. D. & Co., are freely soluble. They dissolve completely in lukewarm water in a very few seconds.

Hypodermatic Tablets, P. D. & Co., are molded by a process that insures firmness. They are not liable to break or crumble in shipping or handling.

Test our hypodermatic tablets with those of any other manufacture. *We invite comparison.*

TUBES OF 25 TABLETS.

With a very few exceptions Hypodermatic Tablets, P. D. & Co., are supplied in tubes of 25. Certain competing tablets are marketed in tubes of 20. Specify "P. D. & Co." on your orders. Get 25 tablets in a tube, not 20.

Home Offices and Laboratories,
Detroit, Michigan.

Parke, Davis & Co.

50 Years of Pharmaceutical Progress

Important Announcement

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES has been authorized to publish from time to time the Official Bulletins issued by the Office of the Surgeon-General.

The JOURNAL esteems it a privilege thus to be of service to the War Department, and is confident that such Bulletins will be of prime interest to our readers.

Note carefully that applicants can apply directly to the Examining Boards and that applications need *not* be forwarded separately to the Office of the Surgeon-General prior to their examination.

INFORMATION RELATING TO APPOINTMENTS IN THE MEDICAL RESERVE CORPS SECTION OF THE OFFICERS' RESERVE CORPS OF THE ARMY

The requirements for appointment are that the applicant be a citizen of the United States, between 22 and 55 years of age, a graduate of a reputable medical school legally authorized to confer the degree of doctor of medicine, he must have qualified to practice medicine in the State in which he resides, and be in the active practice of his profession.

The examination is physical and professional; the professional examination is oral. In case the oral examination is not satisfactory to the Board, the applicant will be given a written examination. In all cases the examination will be in the following subjects:

1. Practice of medicine, including etiology, clinical description, pathology, and the treatment of diseases.
2. Surgery—principles and practice.
3. Obstetrics and gynecology.
4. Hygiene—personal and general, especially as to the prophylaxis of the more prevalent epidemic diseases.
   Specialists will be examined in their specialty.

When a candidate reports to the Board for examination, he should submit the following:

1. His personal history blank properly filled in as indicated therein and certified to before a Notary Public. (This blank will be furnished by the Board if necessary).
2. Two testimonials from reputable persons as to his citizenship, character and habits.
3. A certified copy of his license to practice medicine in the state in which he resides.

The Act of June 3, 1916, creating the Medical Reserve Corps Section of the Officers' Reserve Corps of the Army, provides that in time of peace only those of the grade of first lieutenant may be ordered to active duty, and this with their own consent, but in time of war the services of officers of all grades are at the disposal of the Government.

The pay of officers in the Medical Reserve Corps is the same as that of corresponding grades in the Regular Army.

OFFICE OF THE SURGEON-GENERAL.

Washington, D. C.

OFFICIAL LIST

EXAMINING BOARDS FOR MEDICAL RESERVE CORPS

The following is a list of medical boards as appointed up to June 5. The name and address of the chairman of the board only is given. It is presumed that applicants will select the board most accessible to themselves even though this may mean a board in another State:

ALABAMA

BIRMINGHAM—Capt. John M. Lowrey, M. R. C., 727 1st National Bank Bldg.
MOBILE—Major Eugene D. Bondurant, M. R. C., 166 Conti St.
MONTGOMERY—Major J. N. Barker, M. R. C.

ARIZONA

DOUGLAS—The Surgeon, U. S. Troops.
FT. HUACHUCA—The Surgeon.
NACO—The Surgeon, U. S. Troops.

ARKANSAS

HOT SPRINGS—Commanding Officer, Army and Navy General Hospital.

CALIFORNIA

CORONADO—Major William L. Kneedler, U. S. A., Retired.
LOS ANGELES—Capt. John J. Kyle, M. R. C., 702 Title Insurance Bldg.
SAN FRANCISCO—Commanding Officer, Letterman Gen. Hosp., Presidio, San Francisco.

COLORADO

DENVER—Capt. Cuthbert Powell, M. R. C., Metropolitan Bldg., President.
FT. LOGAN—The Surgeon.
TRINIDAD—Lieut. John R. Espey, M. R. C., Main and Walnut Sts.

CONNECTICUT

NEW HAVEN—Lieut. John W. Churchman, M. R. C.

DISTRICT OF COLUMBIA

WASHINGTON—Commandant, Army Medical School.
WASHINGTON—Major Abram B. Hooe, M. R. C., 1220 Sixteenth St., N. W., President (local only).

FLORIDA

FT. BARRANCAS—The Surgeon.
JACKSONVILLE—Capt. Graham E. Henson, M. R. C., St. James Bldg.
KEY WEST BARRACKS—The Surgeon.
TAMPA—Lieut. E. H. McRae, M. R. C., American Bank Bldg.

GEORGIA

AUGUSTA—Major Eugene E. Murphy, M. R. C., 432 Telfair St.
FT. MCPHERSON—The Surgeon.
FT. OGLETHORPE—The Surgeon.
FT. SCREVEN—The Surgeon.

IDAHO

BOISE—Lieut. Col. Marshall W. Wood, U. S. A., Retired.

ILLINOIS

CHICAGO—Major John A. Hornsby, M. R. C., 111 W. Washington St., President.
MT. VERNON—Capt. William H. Gilmore, M. R. C.
SPRINGFIELD—Capt. George N. Kreider, M. R. C., 522 Capitol Ave.
SPRING VALLEY—Lieut. J. H. Franklin M. R. C.

INDIANA

FT. BENJAMIN HARRISON—The Surgeon.

INDIANAPOLIS—Major George M. Wells, Retired, M. C., 622 Hume-Mansur Bldg., President.

IOWA

FT. DES MOINES—The Surgeon.

KANSAS

EAST HUTCHINSON—Lieut. N. A. Seehorn, M. R. C., 507 Rorabaugh-Wiley Bldg.

FT. RILEY—The Surgeon.

LEAVENWORTH—Lieut. James R. Langworthy, M. R. C., Ryan Bldg.

KENTUCKY

ASHLAND—Lieut. John W. Stephenson, M. R. C.

BOWLING GREEN—Major Arthur T. McCormick, M. R. C.

LOUISVILLE—Capt. Frank T. Fort, M. R. C., "The Atherton."

LOUISIANA

BATON ROUGE—Capt. Charles McVea, M. R. C.

JACKSON BARRACKS—The Surgeon.

NEW ORLEANS—Major Isadore Dyer, M. R. C., 124 Baronne St., President.

SHREVEPORT—Capt. T. P. Lloyd, M. R. C.

MAINE

BRUNSWICK—Lieut. F. N. Whittier, M. R. C., Bowdoin College.

FT. WILLIAMS—The Surgeon.

PORTLAND—Dr. William L. Cousins, 231 Woodford St.

MARYLAND

BALTIMORE—Capt. John S. Davis, M. R. C., 1200 Cathedral St.

MASSACHUSETTS

BOSTON—Major Horace D. Arnold, M. R. C., Harvard Univ. Graduate School of Medicine (President).

FT. BANKS—The Surgeon.

SPRINGFIELD—Lieut. Charles F. Lynch, M. R. C., 387 Main St.

MICHIGAN

ANN ARBOR—Lieut. Reuben Peterson, M. R. C., Univ. of Michigan Med. School, President.

BATTLE CREEK—Capt. W. H. Haughey, M. R. C.

DETROIT—Capt. C. D. Brooks, M. R. C., David Whitney Bldg.

MARQUETTE—Lieut. A. W. Hornbogen, M. R. C.

SAULT STE. MARIE—Lieut. E. H. Webster, M. R. C.

MINNESOTA

FT. SNELLING—The Surgeon.

MINNEAPOLIS—Lieut. James F. Corbett, M. R. C., 4401 E. Lake Harriett Blvd., President.

ROCHESTER—Major Charles W. Mayo, Mayo Clinic.

WINONA—Lieut. Hugh McGaughey.

MISSISSIPPI

HATTIESBURG—Capt. W. W. Crawford, M. R. C.

MERIDIAN—Lieut. I. W. Cooper, M. R. C.

VICKSBURG—Capt. J. S. Ewing, M. R. C.

WINONA—Major J. W. Barksdale, M. R. C.

MISSOURI

COLUMBIA—Maj. Mazyck H. Ravenel, M. R. C., University of Missouri.

FT. WILLIAMS—The Surgeon.

JEFFERSON BARRACKS—The Surgeon.

KANSAS CITY—Major J. F. Binnie, M. R. C., Rialto Bldg.

SPRINGFIELD—Capt. Joseph W. Love, M. R. C.

ST. CHARLES—Dr. Frank J. Tainter.

ST. JOSEPH—Dr. Daniel Morton.

ST. LOUIS—Capt. William H. Luedde, M. R. C., 311 Metropolitan Bldg., Pres.

MONTANA

FT. MISSOULA—The Surgeon.

HELENA—Major William C. Riddell, M. R. C., 504 Dearborn Ave.

NEBRASKA

LINCOLN—Capt. H. W. Orr, M. R. C., 1010 Terminal Bldg.

OMAHA—Col. John M. Banister, U. S. A., Ret., 400 Brandeis Theater Bldg.

NEVADA

RENO—Lieut. Raymond St. Clair, M. R. C., Nixon Bldg.

NEW HAMPSHIRE

HANOVER—Capt. H. N. Kingsford, M. R. C.

MANCHESTER—Capt. J. Franklin Robinson, M. R. C.

NASHUA—Lieut. A. W. Shea, M. R. C.

NEW JERSEY

ATLANTIC CITY—Dr. Gurney Williams, 3915 Atlantic Ave.

NEWARK—Major David A. Kraker, M. R. C., 236 Broad St.

NEW MEXICO

FT. BAYARD—The Commanding Officer.

NEW YORK

ALBANY—Major Henry L. M. Shaw, M. R. C., 361 State St., President.
BUFFALO—Capt. Herbert A. Smith, M. R. C., 566 Delaware Ave.
NEW YORK—Major Henry C. Coe, M. R. C., Academy of Medicine, 17 W. 43d St., President. Office Hours—3 to 5 p. m. every day except Saturday and Sunday.
NEW YORK—Dr. Simon Flexner, 150 E. 61st St.
PLATTSBURG—The Surgeon.
ROCHESTER—Major John M. Swan, M. R. C., 457 Park Ave.
SYRACUSE—First Lieut. Brewster Doust, M. R. C., 641 Park Ave.

NORTH CAROLINA

FT. CASWELL—The Surgeon.
GREENSBORO—Major John W. Long, M. R. C., 119 Church St.

NORTH DAKOTA

BISMARCK—Major E. P. Quain, M. R. C.

OHIO

CINCINNATI—Major Robert D. Maddox, M. R. C., 4 West 7th St., President.
CLEVELAND—Capt. Harry G. Sloan, M. R. C., 1021 Prospect Ave., S. E.
COLUMBUS BARRACKS—The Surgeon.

OKLAHOMA

FT. SILL—The Surgeon.
OKLAHOMA CITY—Lieut. Rex G. Boland, M. R. C., 1524 West 29th St.

PENNSYLVANIA

HARRISBURG—Capt. Benjamin F. Royer, M. R. C., Donaldson Apts.
PHILADELPHIA—Major Elijah H. Siter, M. R. C., 1818 S. Rittenhouse Square, President.
PITTSBURGH—Major John W. Boyce, M. R. C., Empire Bldg., President.
SCRANTON—Lieut. J. Mayhew Wainwright, 516 Spruce St.

RHODE ISLAND

NEWPORT—Lieut. Charles D. Easton, M. R. C., 36 Ayrault St.
PAWTUCKET—Capt. James L. Wheaton, 210 Main St.
PROVIDENCE—Major John W. Keefe, 262 Blackstone Bldg.

SOUTH CAROLINA

CHARLESTON—Col. A. N. Stark, M. C.
COLUMBIA—Lieut. Francis A. Coward, M. R. C., State Board of Health Laboratory.
FT. MOULTRIE—The Surgeon.

SOUTH DAKOTA

ABERDEEN—Lieut. William E. Clark, 519 Seventh Ave., S. E.
STURGIS—Capt. J. D. Brooks, M. R. C.

TENNESSEE

MEMPHIS—Major Frank D. Smythe, M. R. C., 554 East St.
NASHVILLE—Major Lucius E. Burch, Eve Building.

TEXAS

AUSTIN—Capt. Albert F. Beverly, 311 W. 13th St.
DALLAS—Capt. W. H. Moursund, M. R. C., 3004 Thomas Ave.
FT. BLISS—Commanding Officer, Base Hospital.
FT. CROCKETT—The Surgeon.
FT. SAM HOUSTON—Commanding Officer, Base Hospital.

UTAH

FT. DOUGLAS—The Surgeon.

VERMONT

FT. ETHAN ALLEN—The Surgeon.

VIRGINIA

FT. MONROE—The Surgeon.
HOLLINS—Lieut. Allen J. Black, M. R. C.
NORFOLK—Lieut. Burnley Lankford, M. R. C., 530 Shirley Ave.
RICHMOND—Major Stuart McGuire, M. R. C., 513 Grace St., East, President.
WASHINGTON—Major W. D. Webb, M. C., 1803 Connecticut Ave., N. W. (Univ. of Va.). Visits University of Va., Charlottesville, every Thursday.

WASHINGTON

FT. GEORGE WRIGHT—The Surgeon.
SEATTLE—Capt. Ira A. Brown, M. R. C., 901 Seventh Ave.
VANCOUVER BARRACKS—The Surgeon.

WEST VIRGINIA

CHARLESTON—Major John E. Cannaday, M. R. C., Capital City Bank.
HUNTINGTON—Capt. J. Ross Hunter, M. R. C.

WISCONSIN

MILWAUKEE—Capt. C. V. I. Brown, M. R. C., 349 Prospect Ave., President.
SHEBOYGAN—Major E. J. Barrett, M. R. C.

ALASKA

FT. GIBBON—The Surgeon.

PORTO RICO

SAN JUAN—Capt. W. A. Glines, M. R. C., 45 Allen St.

HAWAII

HONOLULU, FT. DE RUSSEY—The Surgeon.

PHILIPPINE ISLANDS

MANILA, P. I.—Commanding Officer, Department Hospital.

SALVARSAN

AND

NEOSALVARSAN

(DIOXYDIAMINOARSENOBENZENE DIHYDROCHLORIDE)—(EHRLICH'S "606")

I AM about to place on the market American Salvarsan and Neosalvarsan, made according to the Ehrlich processes, as carried out by Farbwerke, v. Meister Lucius & Brüning, Hoechst a/Main. It will be made at my new Brooklyn plant, under the supervision of Dr. G. P. Metz, who was instructed in the processes of manufacture at Hoechst.

My plant in Brooklyn, which I have incorporated as the "H. A. Metz Laboratories, Inc.," is nearly completed, and is already turning out Salvarsan, though not yet in commercial quantities. I hope not later than July 1st to supply American Salvarsan and Neosalvarsan to the medical profession and hospitals at a price materially less than that of the imported product, saving the expenses incurred by a duty of 30%, importation charges and royalties.

My plant will be large enough to make the product available also for export to South and Central American countries.

I bespeak the co-operation of physicians in this enterprise, and assure them that no labor or expense will be spared to give them a perfect Salvarsan service.

H. A. METZ, President
Farbwerke-Hoechst Company
H. A. Metz Laboratories, Inc.
122 Hudson Street New York

The Essential Facts about

SARATOGA SPRINGS

All-year American "Cure"

FIRST: SARATOGA SPRINGS LEADS THE WORLD in the therapeutic range of its one hundred and fifty State-owned, naturally charged, radio-active mineral waters.

SECOND: SARATOGA SPRINGS LEADS THE WORLD in the CO_2 gas content of its naturally charged, radio-active Baths.

The following percentage statement of the CO_2 *super-saturation* of the leading baths of the world is based on exact measurements: Nauheim, 25; Homburg, 38; Kissingen, 45; Bruckenau, 50; SARATOGA SPRINGS LINCOLN, 55.

THIRD: THE SARATOGA SPRINGS MEDICAL SANITARIUM, ethically conducted, affords modern creature comforts and modern facilities for diagnosis and dieto-physical therapy.

For analyses of the principal waters and for booklets descriptive of the State Reservation, and the medical resources of Saratoga Springs, address

SARATOGA SPRINGS MEDICAL SANITARIUM

H. E. BARIGHT, M.D., - - Medical Director

SARATOGA SPRINGS, N. Y.

HADDON HALL

ATLANTIC CITY

ALWAYS OPEN

RIGHT ON THE BEACH AND THE BOARDWALK

Appeals particularly to cultivated people who seek rest and recreation at the Sea Shore, Summer or Winter. From every section of the country such guests have come to Haddon Hall for 40 years—and come back again and again—it is so satisfying, so free from ostentation, so comfortable and sufficient. Every facility is offered young and old for enjoyment.

A step and you are in the surf. Fascinating shops and a thousand amusements are offered along the famous Boardwalk. Privileges of fine golf and yacht clubs. Rooms are comfortable and attractive — there is delightful music — and always interesting people.

Make reservations—write for illustrated folder

LEEDS & LIPPINCOTT

NEW (6th) EDITION JUST READY

A MANUAL OF

Materia Medica and Pharmacology

COMPRISING ORGANIC AND INORGANIC DRUGS, ALLIED SPECIES AND USEFUL SYNTHETICS

By DAVID M. R. CULBRETH, Ph.G., M.D.

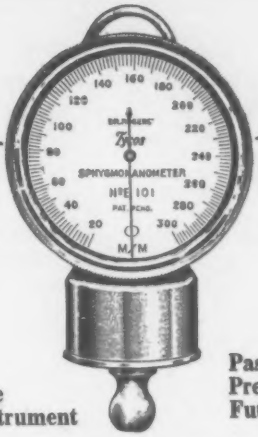
Professor of Botany, Materia Medica and Pharmacology in the University of Maryland.

Octavo, 1001 pages, with 492 engravings. Cloth, $5.25, net.

The author's complete knowledge, thoroughness and accuracy are manifest on every page; and his long experience as a teacher enables him to present the subject in a concise form and clear manner. Thorough revision in accordance with the new U. S. Pharmacopœia has brought this new edition into complete conformity with current scientific thought. This single volume gives physicians and pharmacists a comprehensive and authoritative work on the entire realm of materia medica and pharmacology.

LEA & FEBIGER

706-8-10 Sansom St. PHILADELPHIA PUBLISHERS 2 West 45th Street NEW YORK



The Instrument Past Present Future

DR. ROGERS'
Tycos
SELF-VERIFYING SPHYGMOMANOMETER

Price, in Morocco Case, $25.00
Does away with comparative tests.
A glance *proves* its accuracy.

Taylor Instrument Companies Rochester, N. Y.

Tycos Fever Thermometers, Cambridge Electrocardiograph, *Tycos* Urinary Glassware

THE CHALFONTE is one of the best and most favorably known of all Atlantic City's 1200 hotels. Modern, 10-story, fireproof—its appeal is to cultivated, interesting people seeking rest or recreation at the seashore. It is not a sanitarium

Hepco
TRADE MARK REGISTERED

Flour *for* Diabetes

Palatable

Economical Wholesome

See Joslin's Book
"Treatment of Diabetes Mellitus."

Makes up into a variety of foods — tasty and appetizing. Full directions furnished with every package.

FREE SAMPLE and analysis mailed on request to Physicians

Waukesha Health Products Co.

31 Arthur St. Waukesha, Wis.

NEW WORK **JUST READY**

Mouth Hygiene

A COURSE OF INSTRUCTION FOR DENTAL HYGIENISTS. A TEXT-BOOK CONTAINING THE FUNDAMENTALS FOR PROPHYLACTIC OPERATIONS

Compiled by

ALFRED C. FONES, D.D.S.
Bridgeport, Conn.

Edited by

EDW. C. KIRK, Sc.D., D.D.S., LL.D.,
ROBT. H. STRANG, M.D., D.D.S.,
and
ALFRED C. FONES, D.D.S.

Octavo, 530 pages, with 278 engravings and 7 plates. Cloth, $5.00, net.

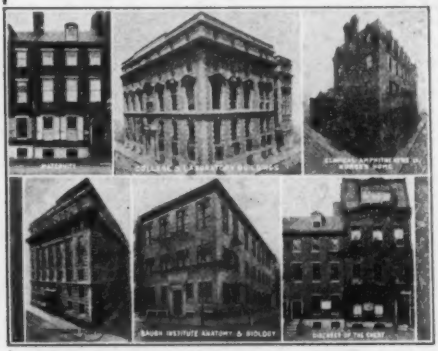
The medical profession fully realizes that unsanitary mouths with diseased teeth are a very potent factor for ill health and systemic infection. Physicians, especially *every medical inspector of schools,* should possess a copy of this work.

LEA & FEBIGER

706-8-10 Sansom St. PHILADELPHIA **PUBLISHERS** 2 West 45th Street NEW YORK

The Jefferson Medical College of Philadelphia

Ninety-third Annual Session Opens September 24, 1917



FOUNDED 1825. One of the oldest and most successful medical schools in America. Has graduated 13,440 physicians; over 5,000 living Alumni. Celebrated for its great clinicians and practical clinical teaching.

ADMISSION: Two years of College Study, including specified language and science work.

FACILITIES: Well equipped laboratories, teaching museums, free libraries, large clinics, the various Departments of the College and its Hospital, with instruction privileges in six other Hospitals, offer advantages of an unusual and superior character.

FACULTY: Eminent medical men of national reputation and unusual teaching ability.

OPPORTUNITIES: All Senior Students may secure interne appointments in the largest and best hospitals; graduates have abundant opportunities to enter various fields.

Circular Announcements descriptive of the Courses will be sent upon request

ROSS V. PATTERSON, M.D., Dean

A Real "Rest" Vacation

Doctor, some of your patients will be needing a vacation soon—a change of scene, restful diversion and a taste of the outdoor life.

Such patients are cordially invited to Battle Creek where everything is scientifically planned for rest, recreation and health-building—where the patient eats, sleeps and lives in a wholesome and "biologic" way.

The bill of fare at Battle Creek is simple, delicious and appetizing. A corps of twenty trained dietitians are always at hand in the dining halls to assist the patient in selecting foods best adapted to his individual needs.

Ample facilities for the outdoor life encourage health-building diversions. Graduated exercises meet the particular needs of the more feeble patients.

If needed, a complete physical examination and treatment are available through the most scientific equipment. Forty specializing physicians, three hundred highly efficient nurses, nearly a hundred trained bath attendants and an able corps of physical directors are at the service of vacationists.

Literature descriptive of the vacation advantages of Battle Creek will be sent free upon request to any physician

THE BATTLE CREEK SANITARIUM

Box 247 :: :: :: BATTLE CREEK, MICHIGAN

Bureau of Chemistry, U. S. Department of Agriculture:

"The spurious aspirin is a mixture of either calcium phosphate and starch, cream of tartar and citric acid with some alum; or milk sugar, starch and calcium acid phosphate."—(From **N. Y. Health Dept. "Weekly Bulletin,"** Nov. 6, 1915.

By Specifying

Bayer-Tablets

AND

Bayer-Capsules

OF

ASPIRIN

(5 grs. each)

The trade-mark "**Aspirin**" (Reg. U. S. Pat. Office) is a guarantee that the monoaceticacidester of salicylicacid in these tablets is of the reliable **Bayer** manufacture.

You Avoid Counterfeits

"Be Sure of Your Aspirin"

"Recent seizures in various cities of the country of numerous quantities of spurious aspirin make it important that the druggist should assure himself in all cases of the reliability of the source of his supply."—**Pacific Drug Rev.**, Feb., 1916.

PASTEUR TREATMENT

MAIL COURSE OF TREATMENT $50.00
(18 doses, with 5 cc glass syringe and needles)

WRITE FOR BOOKLET ON RABIES

PASTEUR INSTITUTE OF ST. LOUIS

R. B. H. GRADWOHL, M.D., Director
928 North Grand Avenue :: :: ST. LOUIS, MISSOURI

Medical Translating and Abstracting

AUDREY G. MORGAN, M.D.

Surgeon General's Library **WASHINGTON, D. C.**

PHILADELPHIA CLINICAL LABORATORY, Inc.

E. Q. ST. JOHN, M. D., President
PROFESSIONAL BUILDING, 1833 CHESTNUT STREET, PHILADELPHIA

GENERAL CLINICAL AND BACTERIOLOGICAL ANALYSES
Autogenous Vaccines—Wassermann's Reaction—Abderhalden's Tests
Analysis of Drinking Water and Milk
Price list and Containers mailed on request

CORNELL UNIVERSITY MEDICAL COLLEGE

IN THE CITY OF NEW YORK

Admits holders of baccalaureate degrees or Seniors who can present a degree at the completion of the first year. All students must have completed College courses in Physics, Chemistry and Biology.
Instruction by the laboratory method continued throughout the course. Classes divided into small sections, facilitating personal contact of student and instructor. Clinical teaching concentrated in those services of Bellevue and New York Hospitals under direct control of Cornell. Additional facilities in other hospitals.
Graduate Courses leading to the degrees of A.M. and Ph.D. are offered in the scientific departments of the Medical College under the direction of the Graduate School of Cornell University.
Session opens the last week in September and closes the second week in June.
Fees, including all college charges, do not exceed $200 a year.
For further information and catalogue address—

THE DEAN, CORNELL UNIVERSITY MEDICAL COLLEGE,
Department C. First Avenue and 28th Street, New York City.

Laboratory of Dr. Allen H. Bunce

ATLANTA, GEORGIA

A modern clinical laboratory well-equipped for making pathological, bacteriological, serological and chemical examinations for physicians and surgeons.

Bleeding tubes, culture media and all other necessary containers furnished free

FOR FEE LIST AND INFORMATION, ADDRESS

ALLEN H. BUNCE, A.B., M.D., Healey Bldg., Atlanta, Ga.

IMPORTANT ANNOUNCEMENT

NEW (2d) EDITION **JUST READY**

THOROUGHLY REVISED AND ENLARGED

THE TREATMENT OF

DIABETES MELLITUS

WITH OBSERVATIONS UPON THE DISEASE BASED UPON THIRTEEN HUNDRED CASES

By ELLIOTT P. JOSLIN, M.D.

Assistant Professor of Medicine, Harvard Medical School; Consulting Physician, Boston City Hospital; Collaborator to the Nutrition Laboratory of the Carnegie Institution of Washington, in Boston.

Octavo, about 550 pages, illustrated. Cloth, $4.50, net.

Dr. Joslin's book has been aptly called "The Clinical Answer to the Allen Treatment." The Rockefeller Institute pronounces it "The best book on the subject."

Dr. Joslin has entirely rewritten the book, presenting an abundance of new material, and giving more detailed instructions for the treatment of the disease, so that it will be easier for the physician independently to care for his patients. Through the kindness of research workers in many large cities, he has been given much information which will also be of distinct help to all interested in the subject.

With this wealth of new material and in view of the remarkable results which have been achieved, and which show conclusively that Diabetes Mellitus is not *per se* an incurable disease, this new edition should appeal even more strongly to the profession, and should be possessed even by those who purchased the first edition.

706-8-10 Sansom St.
PHILADELPHIA

LEA & FEBIGER
PUBLISHERS

2 W. 45th Street
NEW YORK

The Royal Society of Medicine

The Council of this Society offers a cordial invitation to the Commissioned Officers of all the Naval and Military Medical Services, when in London, to make free use of the Society's Rooms (which include Writing, Conference, Smoking, Tea, and Dressing Rooms) and to use the Library for reading and reference.

They are also welcome to attend the meetings which are held for the reading of papers, clinical demonstrations, and for discussions. These are announced in the weekly Medical Journals. The Society's house is open every day, except Sunday, from 11 a.m. to 6.30 p.m.

1, WIMPOLE STREET
CAVENDISH SQUARE, W.

(Principal entrance in Henrietta Street, two minutes' walk from top of Bond St.)

J. Y. W. MAC ALISTER,
Secretary

(To whom all communications should be addressed)

INTERNAL HEMORRHAGE

TRADE

MARK

Easily Controlled

BY

Internal Administration

OF

COAGULEN CIBA

Dissolve contents of a five-gram vial of COAGULEN CIBA in two ounces of Saline Solution or pure water and administer in tablespoonful doses every fifteen minutes until consumed

Quick Action obtained by **intravenous injection** of 20 c.c. of a 3 to 5 per cent. solution of COAGULEN CIBA

Issued by the Society of Chemical Industry in Basle, Switzerland

A. KLIPSTEIN & COMPANY

NEW YORK

A
Rational Procedure
in
Summer Diarrhea

For Infants of any age

Mellin's Food
4 level tablespoonfuls
Water (boiled, then cooled)
16 fluidounces

Give one to three ounces every hour or two, according to the age of the baby, continuing until stools lessen in number and improve in character.

Milk, preferably skimmed, may then be substituted for water—one ounce each day—until regular proportions of milk and water, adapted to the age of the baby, are reached.

THE GLEN SPRINGS

ON SENECA LAKE
OPEN ALL YEAR

WATKINS, N. Y.

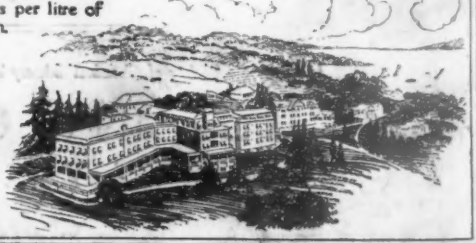
Wm. E. Leffingwell
President

THE AMERICAN NAUHEIM—The Only Place in America Where the Nauheim Baths, so Beneficial to Heart Disorders, Are Given With a Natural Calcium Chloride Brine.

Treatments especially adapted to CARDIO-VASCULAR, RENAL, GASTRIC, NEUROLOGICAL, ENDOCRIN and METABOLIC DISORDERS, NEURITIS, ARTHRITIS, GOUT, OBESITY and allied conditions requiring elimination.

THE BATHS connected directly with the Hotel, are complete with the most advanced equipment. Watkins' Nauheim Spring No. 1 shows very high and constant radio-activity—68 Mache units per litre of water due to Radium Salts in solution.

Diagnostic and treatment methods and equipment are the most advanced which have been approved by medical science.



Ideally perfected conditions for taking "The Cure" the year round

Physicians are requested to send for literature detailing treatments, Mineral Springs analyses and other particulars.